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THE AUGMENTATION OF COLLATERAL CORONARY CIRCULATION BY OPERATION*

FREDERICK R. MAUTZ, M.D., AND CLAUDE S. BECK, M.D.
CLEVELAND, OHIO

IN DECEMBER, 1934, C. S. Beck, V. L. Tichy, and A. R. Moritz[1] reported the first experiments on the production of a collateral circulation to replace the normal blood supply of the heart. Based upon this experimental work Beck[2] devised an operation for treating coronary arterial disease in man and subsequently performed it, with encouraging results, upon twenty-five patients suffering from angina pectoris. Since the beginning of this work, a great many questions have arisen regarding the pathogenesis of heart failure from coronary arterial disease and especially the factors concerned in the spontaneous development of a collateral circulation and the means by which the operative procedure may produce clinical improvement.

It is recognized that the ultimate place of the Beck operation in the treatment of clinical coronary arterial disease will depend upon the comparison of clinical results in comparable groups of operated and nonoperated patients. Inasmuch as the disease is a chronic one, many years must elapse before a final evaluation of the operation can be made. Hence, an attempt is being made through experimental studies to obtain information which will guide the development of the surgical treatment of coronary disease in man. It is recognized that the experiments on dogs are not exactly analogous to the clinical problems, but it is believed that the biologic principles are the same in each group.

The present study has been a continuation of the original experimental work and has been done on dogs. It will not be possible to give here a detailed report of every experiment. Many of the results do not yet lend themselves to statistical analysis. Hence, while single examples

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will be shown to illustrate the discussion of the various points, these examples are presented as characteristic findings of observations which have been repeatedly found on many occasions. In all, this report deals with studies on 297 dogs upon which 458 operations were performed, not counting the experiments originally reported by Beck, Tichy, and Moritz.

The complete solution of the problem of collateral blood flow experimentally would require a quantitative determination of collateral blood flow from the given sources into an ischemic zone of myocardium in the intact, living heart. This problem should be considered from several different aspects:

1. In the normal heart following acute obstruction of a coronary artery.

2. In hearts with partial and complete chronic coronary arterial obstruction.

3. In hearts with chronic coronary arterial obstruction of varying degree in which an operative procedure has been employed to augment the collateral blood flow.

The problem in the normal heart has been in part solved.[3] The complete solution in the heart with chronic coronary arterial obstruction may be technically impossible. There is, however, an indirect approach. The earlier anatomic approach to the collateral circulation in the heart has been proved to lead to fallacious conclusions, since the mere presence of anatomic anastomoses between arterial systems does not prove that there is necessarily an abundant collateral circulation, for blood flow is determined by the resultant of driving pressure minus the peripheral resistance. However, it is believed that increase in size of arterial anastomoses can be interpreted as increased availability of collateral blood flow and that the relative magnitude of available collateral blood supply can be deduced from the relative size and number of collateral channels connecting an ischemic area with various possible sources of blood supply.

A. COLLATERAL CIRCULATION IN THE NORMAL HEART

Before considering the collateral circulation in coronary disease, it is important to know the physiologic capacity of the collateral coronary circulation in the normal heart. Anatomic studies have indicated that there are numerous anastomoses (a) between major coronary arteries,[4] (b) between coronary arteries and extracardiac arteries at the base of the heart,[5] and (c) between coronary arteries and ventricular cavities.[6] In spite of these anatomic connections, most of the evidence indicates an extremely small collateral blood flow into a zone of myocardium made acutely ischemic by ligation of the artery.[7]

However, it seems likely that for a given heart the extent of the anatomic anastomoses may play an important rôle in determining the

outcome of coronary arterial occlusion. Hence, as a basis for the experimental studies of the effects of chronic coronary arterial occlusion, a series of dog hearts were studied to determine the degree of variation of the normal anatomic anastomoses.

Thirty-one normal dog hearts were injected through the circumflex branch of the left coronary artery. The right circumflex branch and the left descendens were ligated at the point of origin just preliminary to the injection to prevent any of the injection mass from entering the ostia of these vessels. A barium sulfate gelatin mixture[8] was found most satisfactory as an injection mass. This mixture consists of 500 gm. barium sulfate, 150 gm. powdered gelatin, and 850 c.c. distilled water. These ingredients are placed in an Arnold sterilizer at 100° C. until completely dissolved. The mixture is filtered while hot through fine linen. Some of the injections were done with an aqueous solution of 0.4 per cent Prussian blue or carmine gelatin under 150 mm. mercury pressure. When it was desired to show the extracardiac anastomoses of the coronary arteries, the thorax was preserved intact, the skin, shoulder girdle, and abdominal muscles being cut away and the cervical and lumbar spine transected. The coronary arteries were approached by resecting a portion of the left fourth rib and sometimes one or two adjacent ribs overlying the heart. Coronary arteries were then cannulated, either by opening the aorta and introducing the cannulas through the aortic ostium or the coronary arteries were dissected free lower in their course. This same technique was used later in the study of the specimens with coronary arterial obstruction. The entire specimen could then be immersed in a warm water bath and warmed to a temperature of 45° C. which would prevent the gelatin from congealing before entering the smallest vessels. The injection bottle and tubing were all completely immersed in the water bath. Injecting was done by building up a pressure of 200 mm. mercury in the injection bottle and releasing the full head of pressure to the coronary artery cannula. The heart was gently massaged during the injection, care being taken not to massage so vigorously as to cause rupture of vessels and extravasation of injection mass. Hearts were either injected immediately after death or after waiting at least twenty-four hours to permit rigor mortis to pass off. During injection the passage of the mass through superficial collaterals into adjacent coronary arteries could frequently be seen by gross inspection; and by later taking sections of these vessels, the size of the anastomosis could be determined at the point of minimum cross-section. Roentgenograms were taken after the specimen was thoroughly chilled to solidify the injection mass. The technique consisted of placing the heart on a cardboard plate holder, six feet from the tube, using a tube of small focal spot and giving an exposure of approximately 100 seconds, with 43 kw. 10 ma.

This study revealed that there was considerable variation in the degree of intercoronary anastomosis in the normal heart (Fig. 1). Separating into arbitrary groups, according to the degree of intercoronary anastomosis, the following results were obtained:

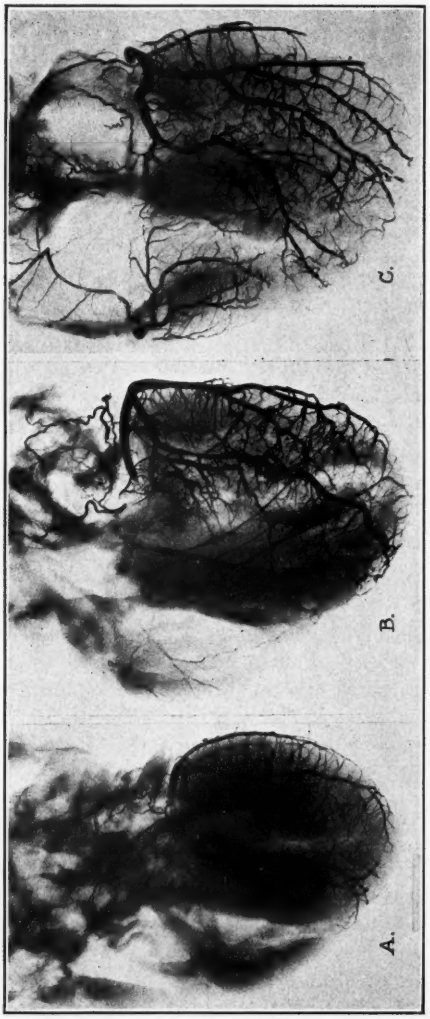

Fig. 1.—Roentgenograms of normal dog hearts which have been injected as described in the text. *A* corresponds to the group showing minimal coronary artery anastomosis. *B* and *C* belong to the group showing maximum anastomosis. *C* was the only heart in this series in which the right coronary artery was completely filled and distended by collateral injection. In *B* the largest anastomosis measured 70 micra in diameter. In *C* it was not possible to trace the anastomoses, but apparently they were only slightly larger than in *B*. Heart *C* has been sectioned so as to show only the posterior half in order to visualize anastomoses between right and left circumflex coronary arteries.

MINIMUM	AVERAGE	MAXIMUM
8 cases (26%)	18 cases (58%)	5 cases (16%)

In 26 per cent of the cases, the injection mass was practically confined to the artery injected with Prussian blue and carmine gelatin,

and entirely so in case of barium sulfate gelatin. In other words, in this group the coronary arteries approach end-arteries in the anatomic sense. In the average groups (58 per cent of the series), there was a slight amount of secondary injection of the right circumflex and descendens areas. In the remaining 16 per cent, the largest intercoronary communications were present. In only one case was the right coronary artery completely filled through the anastomotic channels, and actually distended with barium sulfate gelatin. Careful examination of this heart revealed the largest anastomosis at the point of minimal cross-

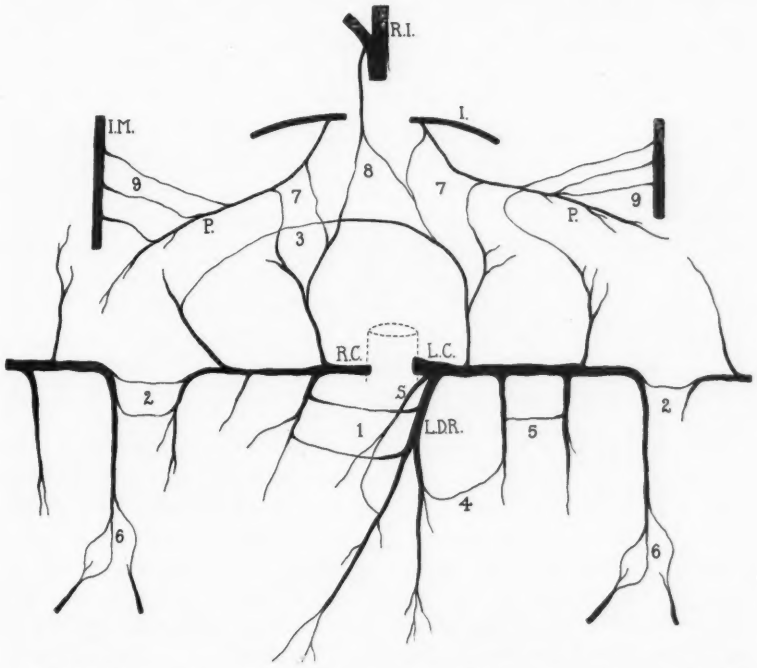

Fig. 2.—Diagram showing anatomic connections between main coronary arteries and between coronary and extracardiac arteries. *R. C.*, right circumflex; *L. C.*, left circumflex; *L. D. R.*, left descending ramus; *S.*, septal; *P.*, pericardial; *I. M.*, internal mammary; *R. I.*, right innominate; *I.*, intercostal. Note the fact that the extracardiac anastomoses in the normal heart are between the small auricular branches of the circumflex arteries and the extracardiac arteries. The common sites of anastomoses are indicated by the numbers.

section to be 70 μ, with the histologic structure of a small artery, an endothelial tube surrounded by single layer of smooth muscle (Fig. 4*A*). The smallest arterioles fill but do not transmit the mass. Capillaries and arterioluminal vessels neither fill nor do they transmit the injection mass.

In ten specimens the heart was injected in situ in the chest, and in each case there was some degree of communication between coronary

and extracardiac arteries as indicated by the extension of Prussian blue from the heart. Only occasionally did the barium sulfate gelatin pass into the extracardiac vessels.

The composite picture of the situations where arterial anastomoses frequently exist in the normal heart is shown in Fig. 2. The actual number of individual anastomoses is much greater in the average heart, and the diagram merely shows the common situations in which these anastomoses occur. Variation in cross-section of the anastomoses is indicated in the previous discussion.

These anatomic studies agree with the blood flow studies of Wiggers[7] and others which indicate that the maximum possible flow of blood through collateral vessels in the beating heart when a coronary artery is acutely occluded is of slight, if any, immediate physiologic significance.

In experiments in which the arterial blood supply to an area of heart muscle is acutely interrupted, contraction of that muscle ceases completely within two minutes and the segment becomes cyanotic and dilates during each systole. When the flow from the peripheral end of a coronary artery which has been completely occluded is collected, it is found to be bright red arterial blood of small minute volume, a few drops per minute. The fact that the blood is bright red in color precludes a significant collateral by retrograde capillary flow.

B. THE COLLATERAL CIRCULATION IN HEARTS WITH CHRONIC OBSTRUCTION OF CORONARY ARTERIES

It was pointed out that following acute occlusion of a coronary artery, the myocardium supplied by the artery rapidly became cyanotic and bulged during systole. In ten dogs that survived right coronary artery ligation, the heart was again exposed at intervals of two to twelve months, and it was noted that the area which following acute arterial occlusion became cyanotic and bulged at the time of the ligation now was of normal color, except for a variable amount of white scar tissue, and the segment could be seen to be actively contracting. In other words, the normal collateral blood supply was generally able to preserve the life of a large percentage of the myocardial fibers until there could be sufficient augmentation of collateral circulation to permit contraction to be resumed.[9] It seems likely that the degree of infarction is inversely proportional to the amount of collateral circulation present at the time of ligation. One would expect the least infarction in the group with the maximum intercoronary anastomoses. It should be pointed out that there has been no way of selecting dogs according to the degree of intercoronary collateral; hence, every experiment has been a random selection, and as such the chance of getting a heart with a maximum degree of both intercoronary and extracardiac anastomosis at the start is small. Thus there is indirect evidence that the degree of anastomosis present in

the normal heart is a factor in determining the end-result of coronary arterial occlusion. This statement refers only to those cases that survive beyond the acute period. Sudden death from ventricular fibrillation may occur following only moderate reduction in lumen of any main artery. In order to produce more extensive coronary arterial occlusion, two methods of gradually occluding the coronary artery were employed: (a) the use of silver bands to compress the main arteries,[10] and (b) the use of a silver screw clamp.[11]

In a group of about 100 dogs an attempt was made to produce chronic progressive obstruction of coronary arteries without producing adhesions between heart and surrounding structures. Following is a typical example of such an experiment.

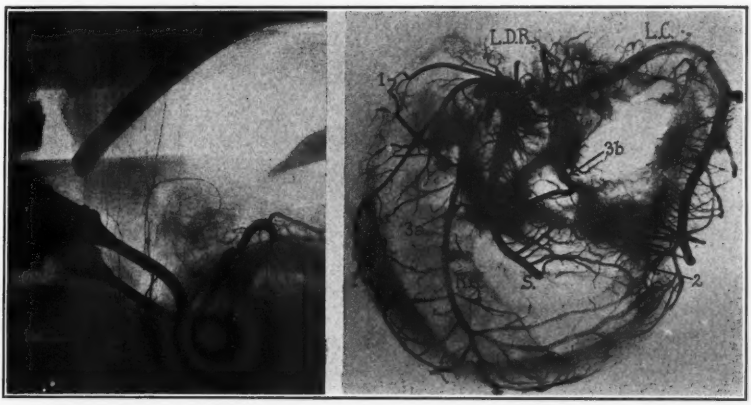

Fig. 3.—Heart 36-91. On the left is a roentgenogram of the base of the heart with the heart in situ in the chest after injection of the coronary arteries. Severe constriction of the main left coronary artery has led to only a slight increase in size of the basal anastomoses which here are principally around the superior vena cava. On the right is a roentgenogram of the base of the heart showing the marked enlargement of the intercoronary communications as indicated by the numbers which correspond to the numbers in Fig. 2.

Left Coronary Artery Obstruction.—Dog 36-91, young male Airedale. July 14, 1936: Screw clamp applied to the main trunk of the left coronary artery above the septal branch. Hemorrhage from posterior aspect of artery controlled by a temporary gauze pack. Screw tightened a half turn to give a snug fit. Aug. 7, 1936: Clamp tightened one and a half turns. Uneventful recovery. Oct. 21, 1936: Clamp tightened, under local anesthesia, one and a half turns, causing pain and change in T-wave. Dec. 30, 1936: Dog found dead. Had been in excellent general condition. Cause of death presumably ventricular fibrillation. Both right and left coronary arteries cannulated through aortic ostia. It was impossible to tell just how much constriction of left coronary artery was present, but it was judged to be severe. Heart injected only through the cannula in the common left coronary artery. The injection mass flowed freely from the right coronary artery, and a pressure of 150 mm. Hg, three-fourths of the injection pressure of 200 mm. Hg, rapidly developed. There was no flow into either ventricular cavity.

Comment.—The free flow of injection mass from the left to the right coronary artery and the ready transmission of pressure indicated that relatively large collateral connections were present between the right and left coronary arteries. Roentgenograms of the heart in situ showed a slight but definite increase in the basal anastomoses, particularly around the superior vena cava. However, the total cross-section of these channels could not have been very great because the injection mass did not escape readily from these channels.

Roentgenograms of the heart (Fig. 3), after removal from the chest, showed several large anastomotic channels between right and left coro-

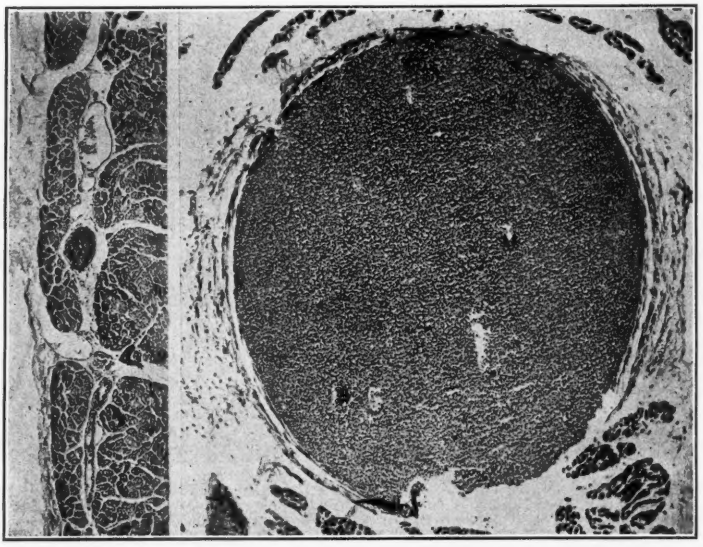

Fig. 4.—Photomicrographs of anastomoses, each magnified 185 times. On the left is one of the largest anastomoses found in the normal heart, *B* of Fig. 1. On the right is a section taken through the interauricular anastomosis at point *3b* in Fig. 3. The histologic structure of the latter in no way resembles an artery, but it was found by dissection that this vessel connected the left proximal auricular artery with the right distal auricular artery, thus serving as a large collateral channel to transport blood from the right to the left coronary artery.

nary arteries: (1) between right distal auricular branch and left proximal auricular branch over the base of the heart; (2) over the conus of the right ventricle; (3) between the right and left coronary arteries in the posterior auriculoventricular sulcus. These anastomoses were verified by dissection. There was no infarction in the region supplied by the left coronary artery.

Histologic examination of these anastomotic vessels showed them to be very thin walled and to contain little smooth muscle and no demonstrable elastic tissue (Fig. 4*B*). This enlargement is apparently two

dimensional, leading to dilatation and elongation with resulting tortuosity. Measurements of the size of the collateral channels at the points indicated in Fig. 3 give the following figures:

	DIAMETER IN MICRA	AREA SQ. MM.	INCREASE IN CROSS-SECTION
Normal heart, No. 36-71	58	0.0026	
Normal heart, No. 36-101	70	0.0040	
Anastomoses in heart, No. 36-91			
1. Conus	528	0.218	55x
2. Conus	493	0.191	48x
3. Interauricular (Fig. 4)	968	0.733	185x
4. In posterior auriculo-ventricular sulcus	968	0.733	185x

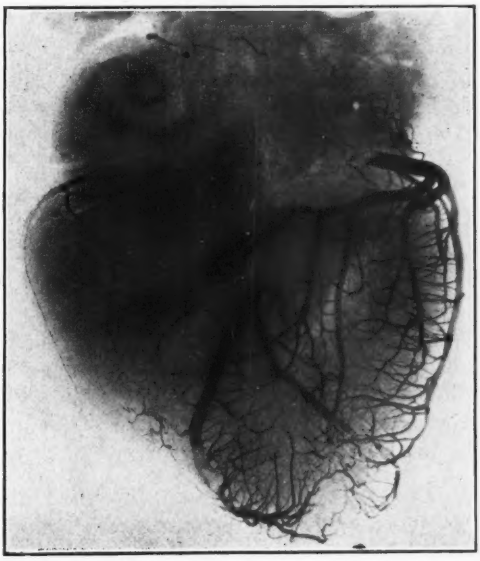

Fig. 5.—Heart 36-108. Right coronary artery was ligated six months previous to death. Autopsy showed almost complete infarction in the area originally supplied by the occluded artery. There was no significant increase in anastomosis between right and left coronary arteries as indicated by poor collateral filling of the right coronary in the roentgenogram.

There may have been other anastomoses which were not discovered, but these alone should permit a tremendous increase in intercoronary collaterals over the normal insignificant amount.

The adjustments for this degree of coronary disease were the widening of intercoronary anastomoses. It cannot be denied that new intercoronary connections developed, but there are adequate connections in the normal heart to account for the collaterals which developed under such conditions. This is an example of a heart in which collaterals develop readily.

There has been considerable speculation as to the nature of the stimulus which leads to widening of collateral arterial channels. Of course, the obvious physical factor is that following occlusion of an artery a gradient of pressure is established between the nonoccluded and occluded artery. That this alone is not sufficient is indicated by the following experience. A number of hearts have been found with extensive, almost complete, infarction below the point of arterial ligation. Injection studies of these hearts failed to reveal more than a slight increase in size of the anastomoses with the occluded artery (Fig. 5). Inasmuch as the metabolic requirements of scar tissue are very low compared to functioning myocardium, it is not surprising that large collaterals failed to develop. This suggests the possibility that there may be a chemical or metabolic factor elaborated in the ischemic area which exerts an influence on adjacent arterial anastomoses. In the process of infarction there is also a great reduction in capillary bed in the infarcted area. This may limit the flow of blood within the infarcted zone which would secondarily reduce inflow through collateral channels and in this way fail to stimulate enlargement of collaterals. These concepts are important in the experimental production of collateral circulation; because if a maximum collateral circulation is to be developed, the rate of occlusion of the arteries must be such as to produce a minimum of infarction.

There probably are intrinsic factors in the tissue which affect the enlargement of collaterals. Perhaps the most obvious of these is related to the age of the individual. In the experimental work we have not studied this problem specifically. Most of our experimental animals were young and on the basis of this might be expected to develop collateral readily, but we have frequently noted the development of excellent collateral in very old dogs.

C. THE RÔLE OF FACTORS INTRODUCED BY OPERATION IN THE CASE OF THE HEART WITH CORONARY ARTERIAL DISEASE

The previously outlined study of the spontaneous development of a collateral circulation in the heart indicates that the enlargement of the intercoronary anastomoses is an extremely important mechanism of compensation in the early coronary arterial obstruction. It also seems quite likely, as has been pointed out, that the degree of intercoronary anastomosis present in the heart before the onset of coronary arterial disease is an important factor in determining how readily spontaneous collateral circulation will develop. It seems quite possible that the epicardial injury produced at the time of the operation may lead to new intercoronary communications, when the injury is produced at the junction between obstructed and nonobstructed coronary arteries. As granulation tissue proliferates to repair an injury, new arterioles develop and in this way new arterial communications may form between

two coronary arteries. The persistence of these vessels probably depends upon a pressure gradient which will maintain an active flow of blood from a normal to an obstructed artery after the injury has healed and the inflammatory process has subsided. This is presented as a hypothesis. To prove this point it would be necessary to demonstrate that intercoronary anastomoses can be created in situations where they do not exist normally. A crucial experimental proof is extremely difficult because of the wide variation in the sites of the normal intercoronary anastomoses. A second hypothesis is that the hyperemia and postoperative tissue reaction of the healing process may exert an influence upon the collateral channels already established in coronary arterial disease. This seems likely but again is very difficult to evaluate experimentally.

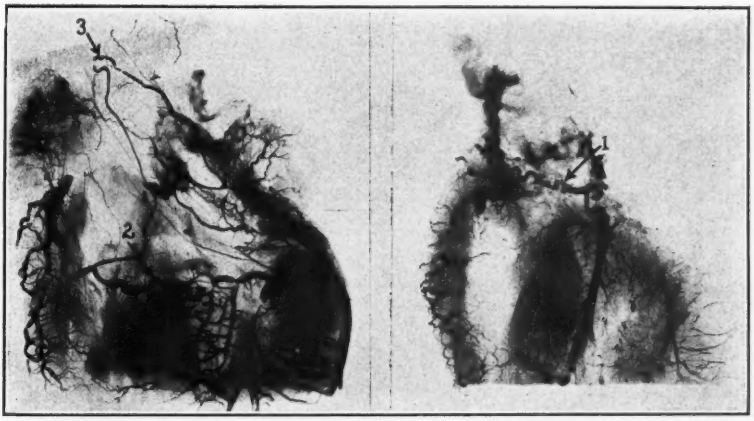

Fig. 6.—Dog No. 35-39. Note the large collateral channels which have developed between the right and left coronary arteries as indicated at *1*, *2*, and *3*. The slight breaks in the arteries are due to cutting during dissection or settling out of the barium sulfate suspension from the gelatin. Here the intercoronary collateral compensated for the arterial obstruction to a large extent.

The remaining factor is the production of new extracardiac anastomoses. In the earlier experiments reported by Beck and Tichy,[10] a measure of the minimal cross-section of the extracardiac anastomoses was obtained by injecting an aqueous dye through these connections into the heart. It was definitely shown that this minimal cross-section of the extracardiac collaterals increases in the presence of chronic obstruction of the coronary arteries. However, this method gives no measure of the relative size of the *basal collaterals*, on the one hand, and the *parietal collaterals* in grafts on the other hand. In order to differentiate these two sets of collaterals, the direction of the injection was reversed and the coronary arteries were injected.

Barium sulfate gelatin was found more satisfactory than aqueous solution of Prussian blue, since it penetrates only the arterial system

and any extension of the mass from the heart must be through direct arterial connections. These injections show that arterial connections were obtained between coronary arteries and the surrounding arterial systems through the adhesions produced at operation. These connections when first developed are of arteriolar caliber and at this time cannot be a very significant source of collateral blood supply. However, what actually happens to these connections once they are created is beyond the control of the surgeon and depends entirely upon those not too well understood factors that determine the spontaneous development of collateral circulation. For example, in many of the experiments the anastomoses present in adhesions were disappointing in spite

Fig. 7.—No. 35-175. This heart was injected through the left descending ramus, *L. D. R.* The left ventricular wall and septum were cut and the heart unrolled to avoid superimposing main arteries. Note the complete filling of the other coronaries through large intercoronary collaterals at *2, 3, 4,* and *6,* and also the filling of the extracardiac vessels, particularly the internal mammary arteries, *I. M.*

of the fact that severe obstruction of the coronary arteries had been produced. The reason is apparent; viz., the adjustments within the heart were sufficient to compensate for the disease. A typical example of this is Dog 35-39.

Dog 35-39.—March 2, 1935: Collateral vascular bed given to the heart; pericardium, skeletal muscle, pericardial fat grafted to epicardium. Left ventricle brought to chest wall. May 15, 1935: Descending ramus ligated one stage. March 9, 1936: Silver band on circumflex, reducing lumen about 60 per cent. Nov. 5, 1936: Sacrificed. Right coronary artery and left circumflex cannulated without disturbing adhesions. Barium sulfate gelatin, introduced into left circumflex, flowed freely from right coronary artery and rapidly built up pressure to 147 mm.

Hg (injected pressure 200 mg. Hg). Roentgenograms of chest and heart showed no filling of extracardiac vessels. Roentgenograms of the heart showed marked enlargement of intercoronary vessels between right and left coronary arteries similar to Dog 36-91 (Fig. 6). Dissection of the heart verified the anastomoses. The left descending ramus was found to be completely occluded near its origin and the left circumflex had only a pinhole lumen at the site of the band, 1.5 cm. from the origin.

In other words, our random selection plus the selection based upon survival of multiple operations tends to leave us with hearts that are so readily able to compensate for arterial obstruction by intercoronary

Fig. 8.—Dog 35-195. Arterial obstruction plus a graft of omentum, showing arterial anastomosis between coronary arteries and arteries in graft. There is also a slight increase in basal anastomosis and a large intercoronary anastomosis over the apex.

collateral that they do not correspond to the selected group of hearts in patients with angina pectoris. Rather they correspond to the hearts with severe coronary arterial disease not giving rise to chronic symptoms. In fact, the animals that develop collateral poorly, corresponding to patients with angina pectoris, tend to be eliminated early in the experiment by fatal result of an operation.

We have attempted to determine how new extracardiac anastomoses can best be produced. Pedicle grafts of the substernal muscle were dis-

appointing because the denervated skeletal muscle fibers became atrophic, and the pedicles became converted into scar tissue and an abundance of collateral channels failed to develop. This was also frequently true when the apex became adherent to the intercostal bundles, and, therefore, was not owing to the fact that the skeletal muscle was denervated. However, in several instances excellent collateral connections were obtained between the coronary arteries and the arteries of the chest wall (Fig. 7).

EXPERIMENT 35-175.—Black and white young male hound, 11.4 kg. Oct. 9, 1935: Operated from right side of chest and right substernal muscle with internal mammary vessels transplanted to right side of heart after roughening epicardium. Oct. 24, 1935: Reoperated from left side. Left coronary artery dissected free and silver bands placed on left circumflex and left descending ramus near bifurcation of the left main artery. The bands produced moderate but definite constriction. The left substernal muscle with internal mammary vessels was then transplanted to heart after roughening the epicardium. Pericardial fat sutured to apex. June 3, 1937: Animal had been in good health but died suddenly one hour after having been fed. Autopsy: Heart and anterior chest wall removed without separating adhesions. Left descendens cannulated, left and right circumflex vessels ligated, and heart injected through the descendens with barium sulfate gelatin. There was free flow of the injection mass from both internal mammary arteries, indicating relative large arterial connections with the coronary arteries.

Roentgenograms of the specimen showed filling of all the coronary arteries and arteries in the grafts (Fig. 7). Dissection of the arteries at the point of constriction by the bands revealed the left circumflex to have been completely occluded by scar tissue. This must have been a gradual process. The ramus descendens was still sufficiently patent to admit a fine probe, but due to scar was much narrower than at the time the band was originally placed around the vessel. There was no infarction of the left ventricle.

The gradual reduction in lumen of the coronary artery by scar tissue around the silver bands was compensated by enlargement of intercoronary anastomoses, as indicated by *2, 3, 4,* and *6* in Fig. 7, and extracardiac anastomoses with the vessels in the graft. The exact connections between coronary and extracoronary vessels cannot be identified in the roentgenogram. That they were relatively large was indicated by the free flow of barium from the internal mammary arteries at the time the heart was injected. The degree of extracardiac anastomosis in this heart was far in excess of any basal extracardiac anastomosis ever seen in hearts with the same degree of arterial obstruction but without grafts. There can be no reasonable doubt that blood was flowing from the internal mammary arteries into the heart during life. The reason such a picture has not been obtained more often probably is the technical difficulty of producing slow progressive occlusion of the coronary arteries. This was accomplished in this case by scar tissue developing around the silver bands.

Adipose tissue has been most promising for developing new arterial connections with coronary arteries, since the anastomoses develop with more regularity than when skeletal muscle is used. In the experiments pericardial and mediastinal fat and omentum have been used. Following is an example of such an experiment.

EXPERIMENT 35-195.—Nov. 5, 1935: Collateral vascular bed produced by grafting omentum to the heart. Nov. 18, 1935: Reoperated, artery believed to be descendens ligated. Severe pain postoperatively and definite electrocardiographic signs of anterior and apical infarct. Recovery. Dec. 14, 1935: Reoperated. Left circumflex ligated. Again severe postoperative pain and marked electrocardiographic changes indicating posterior and basal infarction. Jan. 13, 1936: Band placed on right coronary artery, severely reducing the lumen but probably not completely occluding the vessel. Followed by pain and electrocardiographic changes. Nov. 10, 1936: Sacrificed. Injected through coronary arteries. Roentgenograms (Fig. 8) showed many small arteries in the graft communicating directly with the coronary arteries. There was also marked increase in filling of the vessels anastomosing with the coronary arteries at the base of the heart. Dissection of the coronaries revealed the left circumflex to have been completely occluded; right had pinhole lumen at the site of the band. However, the main branch of the descendens was still patent, a smaller vessel having been ligated at the second operation.

We do not at present have enough information to state whether the anastomoses through the grafts can exceed the size of the basal collaterals. These collaterals have not as yet been studied in serial section. In some of our present specimens the basal collaterals appear in roentgenographic studies slightly to exceed the parietal collaterals in size, but the parietal vessels exceed the basal vessels in number. No claims are made as to the amount of blood that can be transported to the heart through these new vessels. However, the observations indicate that in the late stages of coronary arterial obstruction blood actually flows into the heart through the extracardiac anastomoses, since it is only in severe coronary arterial obstruction that these vessels have been seen to persist and enlarge. No practical solution of this can be reached until human hearts have been studied at various postoperative periods.

Additional study has been made on the method of producing adhesions. The matter of using chemical irritants has been investigated with the same conclusion being reached as previously stated by Beck and Tichy.[19] Such solutions as 1 to 5 per cent silver nitrate and Dakin's solution were painted on the epicardium and parietal pericardium. The reactions were extremely variable, but the fatal outcome of many precludes the clinical use of such irritants in human patients. As little as 1 c.c. of 1 per cent silver nitrate has produced fatal acute compression of the heart when the pericardium was tightly closed. It was noted that these reactions were less severe when the pericardium was opened widely so as to allow drainage into the pleural cavity. Finely powdered reduced iron kaolin gave similar results.

Horse serum and hypertonic sodium chloride solution (10 per cent), while they produced some thickening of the epicardium, did not lead to a satisfactory reaction. Gum acacia gave a more satisfactory reaction, consisting of a subacute type of pericarditis with persistence of a marked hyperemia of the pericardium ten days to two weeks after the introduction into the pericardium. Finely powdered beef bone was next tried and found to give a similar reaction. It was found that this was a relatively bland foreign body which led to a slow and slightly prolonged pericardial reaction without leading to compression of the heart. It was also found that such a reaction in the pericardium does not result in new arterial connections between the coronary and pericardial arteries under normal conditions and hence cannot be substituted for the mechanical burr.

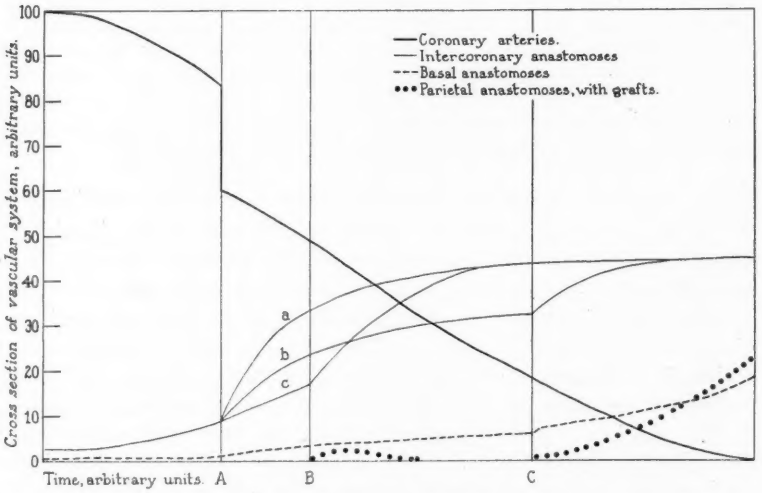

Fig. 9.—Schematic representation of vascular changes associated with chronic progressive coronary arterial obstruction. See text for explanation.

SUMMARY

An attempt has been made to summarize the work in graphic form in Fig. 9. The coronary arteries are assumed to be gradually reduced in lumen, main branches being affected in sequence rather than simultaneously, as indicated in the heavy solid line. The effect of a sudden occlusion, such as might result from a thrombosis, is indicated at time *A*. As the reduction in lumen progresses, the intercoronary anastomoses enlarge, as indicated in the light solid line. After the sudden accident at *A*, several courses are outlined: (a) rapid increase in size of intercoronary anastomoses which compensates to a large extent for the obstruction, (b) an intermediate course, or (c) a poor response. Persistent symptoms are believed to be associated with the latter course. This

might lead to relatively early operation at time *B*, at which time complete occlusion is limited to one main branch. Operation at this time might be expected to improve principally the intercoronary anastomoses (a) by dilatation of existing channels and (b) by the establishment of new intercoronary communications which now may gradually enlarge. The only extracardiac anastomoses which would be likely to develop and survive are those in grafts placed directly upon the localized ischemic area and even these might not significantly enlarge, as indicated by the dotted line, or might regress if the intercoronary adjustments were adequate. In the case of the intermediate course, symptoms are interpreted as occurring much later, say with two main coronary arterial branches occluded. The total blood supply available through the remaining artery and the distribution of the blood to all parts of the myocardium through enlarged intercoronary anastomoses were adequate until there was beginning obstruction of this last main artery. Operation at this time might be expected to slightly improve intercoronary communications and establish new extracardiac anastomoses which would be in a position to persist and continue to enlarge as the coronary disease progressed. It is indicated that the new extracardiac anastomoses might even exceed the basal anastomoses. No place has been given in this chart to the thebesian vessels since there has been no indication in the hearts studied of any anatomic enlargement of these vessels, the criterion used as the indication of the development of collateral circulation.

The authors wish to thank Dr. Alan R. Moritz for valuable suggestions and criticisms throughout the course of this work.

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DISCUSSION

DR. C. S. BECK, Cleveland, O.—The studies presented by Dr. Mautz are the results of a two-year period, during which he has devoted his entire time to these problems. To those of you who have not done any experimental work on the coronary blood supply to the heart, the yield from this study might appear to be rather meager. I believe, however, that these results are very important, because they are going to constitute the foundation for additional work that will be done on this very important subject.

It is extremely difficult to arrive at conclusions in this work. We have had the experience, on a number of occasions, of arriving at what we thought was a conclusion based upon a dozen or two dozen experiments, only later to find that the conclusion became only assumption after a hundred or two hundred experiments were done. So we must be careful, always, in arriving at conclusions.

You might perhaps want to know about the results on the human patients up to the present time. We have operated upon 25 patients, who had coronary disease, for the purpose of improving the circulation in the heart muscle. Of these 25 patients, we have lost 8 and had 17 recover. In the first 14 operations that were performed, the mortality was 50 per cent. In the last 9 operations that were done, the mortality was 0.

The requirements for this operation are as follows: First, the patient must show unequivocal coronary sclerosis. He must show electrocardiographic evidence of coronary disease.

The second requirement is that the patient cannot get along with any degree of satisfaction or comfort on medical therapy or on complete physical and mental rest.

The third requirement of the operation is that the patient should not be in circulatory failure. We deviated from that rule once, and I operated upon a patient with extreme coronary disease, who was in failure. I knew the patient could not stand much in the way of an operative procedure, and all I did was to take out one costal cartilage, open the parietal pericardium, and insert 5 gm. of powdered beef bone for the purpose of increasing intercoronary communications, or for the purpose of adding new capillary anastomoses from the pericardial fat. This patient stood the operation. He remained in failure after operation and died four months later. Autopsy was not obtainable. The operation was an incidental thing in his course. I think it did not do him any good, but I think it did him no harm.

A patient who is in failure with coronary disease has nothing to offer the surgeon. He has nothing to work with, and I think such patients should not be accepted for operation.

We might classify the remaining 16 patients, then, into three or four groups. In the first group we will place those patients who have been absolutely and completely relieved of pain. They take no drugs. They are stronger, and they say they feel fine. A result like this is really not to be expected when we consider the type of disease with which we are dealing. How can any augmentation of arterial blood supply affect myocardium that is once fibrotic? We cannot expect such a result. However, we have 3 patients in this group—no pain, no drugs, and they say they are well.

The larger group consists of patients who have had pain relieved to a certain extent. They have reduced the amount of medication to a very great extent. Some of them are taking no medication. Their capacity for exercise has increased; some of them are working. In this group we have 9 patients.

The third group is one in which the improvement is slight, reduction of pain slight, increase in activity slight, medication still continued, but not as much as

before, and in this group we have 1 patient. This patient, I am sure, has extensive damage in the heart muscle of a permanent nature. I doubt whether he was a good candidate for the operation.

The fourth is a group in which there is no improvement, no increase in exercise tolerance, and in this group we have no patients.

There are 3 patients not accounted for in this summary, and these 3 have been operated upon within the last four months. They have not gone quite long enough for us to make an appraisal of them, but they are all improved.

In conclusion, I simply want to say that the results so far obtained by this work are encouraging. We must give it time; we must carry out more studies.

DR. F. R. MAUTZ, Cleveland, O.—Regarding the question brought up by Dr. Graham, I wish to state that we believe one of the necessary conditions for the persistence of the larger new arterial anastomoses is a pressure gradient between arterial systems joined by the granulation tissue. We cannot as yet say what the result will be when such an operation is produced several years in advance of the arterial obstruction.

I should like to refer to some work recently completed in which, in collaboration with Dr. Donald E. Gregg, of the Department of Physiology, the peripheral pressure of chronically occluded coronary arteries has been measured. In acutely occluded coronary arteries, the peripheral pressure measures approximately one-fifth of the aortic pressure. In the chronically occluded arteries the pressure has been observed to be as much as four-fifths of aortic pressure and the back flow of blood from the periphery of the occluded artery about 150 times what one would expect in an acute arterial occlusion. Thus there can be no room for doubt that a massive collateral circulation can and frequently does develop following occlusion of coronary arteries. We hope this method of study will in time lead to a quantitative objective evaluation of what an operative procedure will do to augment the collateral coronary blood supply.

TUBERCULOUS PERICARDITIS*

ALFRED BLALOCK, M.D., AND SANFORD E. LEVY, M.D.
NASHVILLE, TENN.

TUBERCULOSIS follows hard upon rheumatic fever as a cause of pericarditis. The affection is usually overlooked clinically, and possibly in some cases anatomically. In 1,000 autopsies, the majority of which were made at the Montreal General Hospital, there were 275 cases with tuberculous lesions, in seven of which the pericardium was involved.'' Thus wrote Sir William Osler[1] in 1893. Norris[2] found 1,780 cases of tuberculosis, 82 of which had tuberculous pericarditis, in 7,219 autopsies in Philadelphia hospitals. Kornblum, Bellet, and Ostrum[3] state that the incidence in general autopsies of tuberculous pericarditis is approximately 1 per cent and that tuberculous involvement of the pericardium occurs in about 4 per cent of autopsies on patients with pulmonary tuberculosis. Graham, Singer, and Ballon[4] state: ''That tuberculous pericarditis is not infrequently met with in the young is well known. In the aged, tuberculosis is the most common cause of pericarditis. In 3,000 post-mortem examinations performed on individuals over 60 years of age, Christ noted its occurrence on 69 occasions. The total number of cases of pericarditis in this series was 169.''

The purpose of this communication is to report the cases of tuberculous pericarditis which have been observed in the Vanderbilt Hospital in the past eleven years. Most of the reports in the literature deal with autopsy findings. An exception is a recent excellent article by Harvey and Whitehill.[5] They state: ''During the past 45 years, 95 cases of tuberculosis of the pericardium have been admitted to the Johns Hopkins Hospital. Of these, there were 71 which were clinically important, of which 37 were proven and 34 unproven. The unproven cases resembled in every respect the proven ones. However, certain differences do exist between the proven and unproven ones. Of 20 proven cases with effusion 16 or 80 per cent died, and 15 of the 17 proven cases without an effusion succumbed, making a total mortality of 83 per cent. This is striking contrast to the death rate of only 5.9 per cent for the 34 unproven cases.'' We have found it advisable to group our patients somewhat differently because pericardiectomy was carried out on a few of them.

Forty-two patients have been observed in this eleven-year period in whom a diagnosis of tuberculous pericarditis either was proved or strongly suspected. Twenty-four belong in the former category and 18 in the latter. A number of patients (10) in whom it was considered that there was a remote possibility of tuberculous pericarditis are not in-

*From the Department of Surgery of Vanderbilt University.
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cluded. Also not included are a group of patients who at autopsy were found to have chronic adhesive pericarditis, the cavity obliterated, the fine fibrous adhesions readily broken, and who were found to be without evidence of active tuberculosis in the pericardium. A total of 1,653 autopsies were performed in the hospital during this eleven-year period.

The cases are divided into the four following groups for purposes of analysis: (I) patients with active tuberculous constrictive pericarditis on whom pericardiectomy was performed (6 cases); (II) patients in whom tuberculous pericarditis was the chief cause of death and on whom pericardiectomy was not performed (7 cases); (III) patients with proved tuberculous pericarditis, in whom it was a contributing but not a chief cause of death (9 cases); and (IV) patients in whom tuberculous pericarditis was strongly suspected but not proved (18 cases). Perhaps conspicuous by its absence is a group which might include patients in whom a positive diagnosis has been made and who are living without having had a pericardial resection. Only 1 patient meets these requirements, and he is extremely ill at the present time. In other words, every patient, with one exception, with a proved diagnosis of tuberculous pericarditis, and who has not had a pericardiectomy, is dead.

Group I. Patients With Active Tuberculous Constrictive Pericarditis on Whom Pericardiectomy Was Performed.—This group, comprising 6 patients, is probably the most interesting of the series. Two patients, who were operated upon and who have been reported by Bigger, are not included. One of these probably does not fit into the present classification, since an active infection was not demonstrated in the pericardial scar, but the patient had tuberculous peritonitis. This patient is entirely well at the present time, eight years following pericardiectomy. It was necessary to interrupt the operation on the second patient because of hemorrhage. Those patients who have had a pericardial resection for causes other than a proliferative tuberculous infection are not included here and will be reported in association with C. S. Burwell.

The 6 patients were males and all had been sick at the time of the operation for months rather than years. With one exception, the patients were forty years or more of age. Several of them were observed frequently from the time that the effusion developed until most or all of the fluid disappeared and the pericardial surfaces became markedly thickened. The chief complaints in most instances consisted of dyspnea on slight exertion and cough. All of the patients had prominent veins, an elevated venous pressure (195 to 300 mm. H_2O), a paradoxic pulse, a low pulse pressure, distant heart sounds, a fixed heart with little or no visible pulsation under the fluoroscope, an enlarged liver, pleural effusion, and ascites. Some of these findings are enumerated in Table I.

A decision to operate was usually made on the grounds that the patient was becoming sicker and the venous pressure was rising despite the fact that the heart-pericardial shadow had become smaller. A

TABLE I

PATIENTS WITH ACTIVE TUBERCULOUS CONSTRICTIVE PERICARDITIS ON WHOM PERICARDIECTOMY WAS PERFORMED*

PATIENT	AGE SEX	COLOR	CHIEF COMPLAINTS	DURATION ILLNESS	VENOUS DISTENTION AND PRESSURE MM. H_2O.	PLEURAL EFFUSION	ASCITES	DIMINISHED PULSATION HEART	PARADOXIC PULSE	RESULT
1	18	C	Dyspnea	2+ mo.	+	+	+	+	+	Two operations; 1+ years since last; cured
J. O.	M		Cough		300					
2	40	W	Dyspnea	7 mo.	+	+	+	+	+	Greatly improved; nine months since operation; returned to work
A. H. K.	M		Cough		278					
3	61	W	Dyspnea	5 mo.	+	+	+	+	+	Much improved; nine months since operation
R. H. W.	M		Edema		215					
4	51	W	Dyspnea	4 mo.	+	+	+	+	+	Improved for six months; died miliary tuberculosis
J. W.	M				215					
5	46	W	Dyspnea	6 mo.	+	+	+	+	+	Died shortly after operation; probably acute dilatation heart
B. C.	M		Pain chest		210					
6	45	W	Dyspnea	4 mo.	+	+	+	+	+	Improved temporarily; died 2 months after operation of miliary tuberculosis
E. C.	M		Large liver		195					

*Does not include two patients operated upon and reported by Dr. I. A. Bigger. One of these had a proliferative tuberculous pericarditis and died twelve hours following the operation, probably as result of hemorrhage. The other had a healed pericardial scar and an active tuberculous peritonitis. He is entirely well almost eight years since operation.

marked thickening of the pericardium and epicardium, particularly the former, was found in all instances. Small pockets of fluid, encapsulated between the two thickened and elsewhere adherent layers, were found in 4 patients. The pericardium of 1 (Case 4) showed a moderate amount of calcification. Large areas of the thickened scar were removed in all instances and microscopic study revealed a tuberculous infection with activity.

It was necessary to perform two operations on one patient (Case 1). He improved somewhat following the first decortication but then became worse, and a more extensive resection was carried out six months following the first. The scar removed at the second as well as the first operation showed an active infection. There were no pockets of fluid at the time of the second procedure. The patient's progress has been entirely satisfactory.

One of the patients (Case 5) was almost moribund at the time that he was taken to the operating room. The anesthetist could not obtain his blood pressure. He had been in the hospital three months and his condition had become progressively poorer. The only anesthetic used consisted of local infiltration with novocaine (true also in Case 3). The operation was performed without incident. However, it was observed that there was a stream of blood which spurted from the flap of scar which was freed from the right ventricle. This was controlled without difficulty. The cavity of the heart was not entered. The incision was closed and the patient stated that he felt better than he had before the operation. However, he died very suddenly about fifteen minutes subsequently. This brought up the question as to whether or not the arterial supply to the heart muscle had been impaired in the removal of the scar. This will be discussed subsequently. Unfortunately, the relatives would allow only the reopening of the incision. There had been no bleeding subsequent to the operation.

Three of the 6 patients are cured or greatly improved following the operation. Two have returned to active work and the third goes to his office occasionally. The remaining 3 patients are dead. One of these was definitely improved following the operation but died six months subsequently with miliary tuberculosis. Another patient was somewhat improved for several weeks but died two months following the operation. Miliary tuberculosis was found at autopsy. The third patient, who died a few minutes following the completion of the operation, has been commented upon.

Group II. Patients in Whom Tuberculous Pericarditis Was Chief Cause of Death; Pericardiectomy Not Performed.—This group includes 7 cases. All of the patients died in the hospital and autopsies were performed on 6 of them. It is of interest that all of the patients were males and the youngest of these was forty years of age. The complaints, the duration of the illness, the symptoms and signs were similar

TABLE II

PATIENTS IN WHOM TUBERCULOUS PERICARDITIS WAS CHIEF CAUSE OF DEATH; PERICARDIECTOMY NOT PERFORMED

PATIENT	AGE SEX	COLOR	CHIEF COMPLAINTS	DURATION ILLNESS	VENOUS DISTENTION AND PRESSURE MM. H.O.	PLEURAL EFFUSION	ASCITES	DIMINISHED PULSATION HEART	PARADOXIC PULSE	REMARKS
1 W. K.	40 M	W	Dyspnea	2 yr.	+ 257	+	+	Not done	+	Died 1 day following admission; autopsy showed proliferative pericarditis without fluid; pericardium 1 cm. thick
2 J. B.	51 M	W	Dyspnea Cough	2 mo.	+ 305	+	+	+	+	In hospital 5 weeks; was believed to have effusion but had scar; 15 c.c. fluid, scar 1 cm. thick
3 E. M.	50 F	C	Edema Dyspnea	4 mo.	+ Not done	+	+	+	+	Died 13 hours after admission; proliferative pericarditis without fluid; scar 3 cm. thick at base of heart
4 S. N.	70 M	C	Dyspnea Edema	5 mo.	+ 230	+	+	+	+	Pericardium drained 5 weeks before death; mistake in diagnosis; scar 1 cm. thick at autopsy; several c.c. thick fluid
5 W. J. T.	41 M	W	Weakness Chills	2 mo.	+ Not done	+	+	+	+	Pericardium drained 7 weeks before death; mistake in diagnosis; scar about 1 cm. thick at autopsy, no fluid; also had acute disseminated tuberculosis
6 W. M.	45 M	W	Cough Pain chest	7 mo.	+ Not done	+	+	+	+	Autopsy showed thickening of pericardium and epicardium without fluid; also had acute glomerular nephritis
7 J. D.	42 M	W	Dyspnea Pain chest	8 mo.	+ 200	+	+	+	+	Pericardial fluid contained tubercle bacilli; x-ray showed some calcification; developed miliary tuberculosis shortly before death; autopsy not granted

to those of the patients described in Group I. Some of these are listed in Table II. Drainage of the pericardium had been carried out on two of the patients five and seven weeks, respectively, preceding death, under the impression that the disease was not tuberculous in origin. Large quantities of slightly bloody fluid (400 and 1,000 c.c.) with slight thickening of the pericardium were found at the time of operation. However, at autopsy, the fluid had almost completely disappeared, the two surfaces were adherent in most areas and were approximately 1 cm. in thickness. All of the autopsies showed a marked thickening of the two surfaces without a significant amount of fluid in any case, the largest quantity being 15 c.c. The scar at the base of the heart in Case 3 measured 3 cm. in thickness.

Tuberculous pericarditis was not the only site of an acid-fast lesion in any of the patients. In other words, none of the patients had an anatomically primary tuberculous pericarditis, but most of them had a pericarditis which was primary from the clinical viewpoint. There is confusion in the use of the terms and this point will be commented upon subsequently. All of the autopsies revealed tuberculosis of the mediastinal nodes. There was evidence of an active pulmonary infection in all instances except two.

Two of the patients died after being in the hospital less than twenty-four hours and operation was out of the question due to the extremely poor condition of the patients. One patient (Case 7) developed miliary tuberculosis at about the time that the heart-pericardial shadow began to decrease in size, and it is doubtful if pericardiectomy would have resulted in benefit. One patient (Case 6) had acute glomerular nephritis as well as tuberculous constrictive pericarditis and again operation would probably have been of doubtful value. As has been stated, pericardial drainage was carried out in two patients (Cases 4 and 5). One of these patients had acute disseminated tuberculosis at autopsy. The other patient might have been improved by pericardiectomy. The remaining patient in this group (Case 2) was in the hospital five weeks preceding death and was believed to have pericardial effusion of rheumatic origin. The finding of a thick scar at autopsy, even though activity was still present, indicates that the patient might have been cured by pericardiectomy. In summary, two of the patients in this group might have responded favorably to resection of the pericardium.

Group III. Patients With Proved Tuberculous Pericarditis in Whom It Was a Contributing But Not Chief Cause of Death.—This group includes 9 patients, 8 of whom died in the hospital and were autopsied. The remaining patient died two weeks after leaving the hospital. Seven of the patients were males. In contrast to the previous groups, the ages varied from two to sixty years. The duration of the illness varied in the different patients from two weeks to two and one-half years. The findings on examination varied considerably more than those of the

TABLE III

PATIENTS WITH PROVED TUBERCULOUS PERICARDITIS IN WHOM IT WAS A CONTRIBUTING BUT NOT CHIEF CAUSE OF DEATH

PATIENT	AGE SEX	COLOR	CHIEF COMPLAINTS	DURATION ILLNESS	PAST HISTORY TUBERCULOSIS	PERICARDIAL FRICTION RUB	VENOUS DISTENTION PRESSURE Mm. H_2O	ENLARGED SHADOW X-RAY	PARADOXIC PULSE	B. P. M.M. HG	ASCITES PLEURAL EFFUSION ENLARGED LIVER	PERICARDIAL TAP	CONDITION PERICARDIUM AT AUTOPSY	CHIEF CAUSE OF DEATH
1 J. K.	53 M	W	Cough Chills	2 wk.	No	No	?	Yes	No	109/76	No	No	500 c.c. yellowish fluid with fibrin; thickened pericardium	Acute confluent pneumococcus pneumonia; tuberculosis of various organs
2 E. E.	23 F	C	Dyspnea Edema	3 mo.	No	Yes	Yes	Yes	?	80/60	Yes	Yes Positive	Fluid and thickening both layers; few adhesions	Tuberculous polyserositis; tuberculous bronchopneumonia
3 E. B.	32 M	C	Swelling abdomen	2 mo.	No	Yes	Yes 120	No	No	135/85	Yes	No	Shaggy exudate epicardium; small amount fluid	Acute disseminated tuberculosis
4 K. H.	24 M	C	Pain chest and abdomen	1 mo.	No	No	Yes	Yes	Yes	115/88	Pleural effusion	Yes Positive	Two layers adherent most places, 5 mm. thick	Acute cerebral tuberculous meningitis; miliary tuberculosis

TABLE III—CONT'D

PATIENT	AGE SEX	COLOR	CHIEF COMPLAINTS	DURATION ILLNESS	PAST HISTORY TUBERCULOSIS	PERICARDIAL FRICTION RUB	VENOUS DISTENTION PRESSURE Mm. H_2O	ENLARGED SHADOW X-RAY	PARADOXIC PULSE	B. P. M.M. HG	ASCITES PLEURAL EFFUSION ENLARGED LIVER	PERICARDIAL TAP	CONDITION PERICARDIUM AT AUTOPSY	CHIEF CAUSE OF DEATH
5 J. C.	24 M	C	Pain abdomen	2 wk.	No	Yes	No	Yes	No	110/70	Yes	Attempted	Pericardium thickened, lined with flaky material; tuberculosis myocardium	Hemopericardium following aspiration; one liter of blood at autopsy
6 F. S.	60 M	W	Dyspnea Weakness	5 mo.	No	No	Yes	Yes	No	145/110	Enlarged liver	No	Two layers greatly thickened; 50 c.c. fluid	Acute and chronic pyogenic bronchopneumonia; general arteriosclerosis
7 K. M.	2 F	C	Edema Cough	2 mo.	Yes	No	No	No	No		Yes	No	Tubercles sac opposite caseous mediastinal nodes; tuberculosis heart	Caseous tuberculous bronchopneumonia; miliary tuberculosis
8 A. W.	31 M	C	Dyspnea Cough	1 yr.	No	No	Yes	Yes	No	105/88	Yes	No	No fluid; tubercles; two layers fused and moderately thickened	Cardiac hypertrophy and dilatation; multiple infarcts
9 W. M. B.	45 M	W	Cough Weakness	2½ yr.	Yes	No	Yes 210	No	Yes	115/95	Ascites Enlarged liver	No	Died two weeks after discharge; no autopsy	Bilateral pulmonary and renal tuberculosis and constrictive pericarditis

previous groups. With one exception, all of the patients showed definite signs of systemic congestion. The remaining patient had an acute effusion and was the only one who at autopsy had a large amount of fluid in the pericardial cavity (500 c.c.). Aspiration of the pericardium was attempted in only 3 patients. Two of these yielded fluid which was positive on guinea pig inoculation. The third patient died of hemopericardium shortly following an attempt at aspiration. The chief causes of death were: (1) acute disseminated tuberculosis in 5; (2) acute confluent pneumococcus pneumonia in 1; (3) acute and chronic pyogenic bronchopneumonia in 1; (4) acute cerebral tuberculous meningitis in 1; (5) cardiac hypertrophy and dilatation with multiple infarcts in 1; and (6) hemopericardium in 1. Of the 8 cases which were autopsied, tuberculosis of the mediastinal nodes was demonstrated in all except the patient who died of hemopericardium. The findings in this group are recorded in Table III.

Group IV. Tuberculous Pericarditis Strongly Suspected But Not Proved.—This group includes 18 patients, 15 of which are males. The ages vary from twenty to sixty years. The most frequently encountered complaints were dyspnea on exertion, pain in chest, cough, and edema. The duration of the illness varied from one day to many years. Ten of the patients had a pericardial friction rub. There was definite venous distention in 11 of them, the highest pressure being 310 mm. H_2O. There was an enlargement of the heart-pericardial shadow in 15 of the 18 patients, and it was questionable in another. The remaining 2 patients had a relatively small shadow associated with an undoubted constrictive pericarditis of longer duration. A paradoxic pulse was present in 8 and was questionable in several others. Definite evidence of systemic venous congestion was present in 14. Aspiration of the pericardium was carried out in only 1 patient and the fluid was negative on guinea pig inoculation. One of the patients died in the hospital of pneumonia, four days following an attempt to decorticate the heart. The attempt was abandoned because of hemorrhage; no pericardium was removed; and an autopsy was not granted. Eight of the patients have died since leaving the hospital. Three are partially and 2 are totally incapacitated. Four patients are well or at least are symptom free at present. These patients were not very ill at the time that a diagnosis of acute pericarditis was made, and there is a moderate amount of doubt as to the correctness of the diagnosis.

SUMMARY OF ALL GROUPS

In summary, 42 patients in whom tuberculous pericarditis was suspected or proved have been studied. Thirty-six, or 86 per cent, of the patients were males. Twenty-five were white and 17 colored. The ages ranged from two to seventy years, the average age being 40.3 years. The two-year-old child died of caseous tuberculous bronchopneumonia

and miliary tuberculosis; the pericarditis consisted in the main of a few tubercles opposite caseous mediastinal nodes. She was the only patient in the first decade of life. There were 2 in the second decade, 8 in the third, 5 in the fourth, 13 in the fifth, 9 in the sixth, 3 in the seventh, and 1 in the eighth. Thus, it is to be observed that it is not a disease of youth. This is particularly true of those patients in whom a true constrictive pericarditis due to an active tuberculous infection was proved by operation or autopsy. These comprise the patients in the first two groups and only one of these was less than forty years of age.

Of the 24 patients in whom the diagnosis was proved, all are dead except for 3 patients who are improved following the operation and 1 with subacute pericarditis who is in the hospital at present. In 9 of these, the tuberculous pericarditis was not considered the main cause of death. The patients in whom tuberculous pericarditis was suspected but not proved were in general less ill than the others. Aspiration of the pericardium was attempted in only 1 of these. Only 1 of these patients died in the hospital; this death was due to pneumonia and followed an operation which was not completed because of hemorrhage. Eight of these patients have died since leaving the hospital and only 4 are free of symptoms.

ETIOLOGY

It is generally believed that the pericardium may be infected with the tubercle bacillus in one of three ways: (1) by way of the blood stream, (2) through the lymphatics, and (3) by direct extension from disease in a neighboring structure. Osler[1] stated: "Tuberculous pericarditis is due in a majority of instances to infection of the membrane from caseous mediastinal lymph glands. The disease may be confined to these glands and to the pericardium. . . . Of the 101 instances of disease of the lymph glands of the mediastinum, collected by Bevety, the glands were caseous in the 18 cases in which the pericardium was involved. . . . A second, less common mode of extension is from the pleura or from the lung. . . . And, lastly, there are instances in which the pericardium appears to be involved with the pleura and peritoneum in a general tuberculosis of the serous membranes." Riesman[6] divided tuberculous disease of the pericardium into four groups, as follows: (1) that which is associated with general miliary tuberculosis, (2) that associated with general serous membrane tuberculosis, (3) that due to extension from neighboring structures, and (4) that developing independently. He stated: "The majority of cases of well-marked pericardial tuberculosis are the result of extension from neighboring tuberculous foci, most frequently from the mediastinal and peri-bronchial lymph glands. Weigert, to whom we owe the demonstration of this fact, showed that the pericardial disease, as a rule, has its origin from lymph glands situated on the anterior layer of the pericardium in

TABLE IV

TUBERCULOUS PERICARDITIS STRONGLY SUSPECTED BUT NOT PROVED

PATIENT	AGE SEX	COLOR	CHIEF COMPLAINTS	DURATION ILLNESS	PAST HISTORY TUBERCULOSIS	PERICARDIAL FRICTION RUB	VENOUS DISTENTION	ENLARGED SHADOW X-RAY	PARADOXIC PULSE	B. P. MM. HG	ASCITES PLEURAL EFFUSION ENLARGED LIVER	PERICARDIAL TAP	REMARKS
1 A. T. A.	39 M	W	Dyspnea	3 mo.	No	No	Yes 310	Yes	Yes	85/70	Yes	No	Died 4½ months after leaving hospital
2 J. B.	58 M	W	Dyspnea Cough	6 wk.	No	Yes	?	Yes	?	105/78	Effusion	Yes Negative Guinea pig	Chronic pulmonary tuberculosis; died shortly after leaving hospital
3 W. H.	27 M	C	Dyspnea Cough	1 mo.	No	Yes	Slight	?	Yes	115/90	Yes	No	Tuberculous peritonitis demonstrated; died 3 years after leaving hospital
4 Z. H.	48 M	C	Dyspnea Swelling abdomen	5 mo.	No	Yes	Yes 210	Yes	Yes	115/95	Yes	No	Died 10 months after leaving hospital
5 M. R.	27 F	C	Dyspnea Edema	3 yr.	No	Yes	Yes 200	Yes	Yes	114/90	Enlarged liver	No	Patient has been followed since effusion developed 3 years ago; partially incapacitated at present; V.P. rising
6 C. N.	20 M	W	Pain chest	1 day	No	Yes	Yes 145	Yes	Yes	100/68	No	No	Calcified hilus glands; 1 year since onset; no symptoms at present
7 J. S. R.	54 M	W	Dyspnea Pain	10 yr.	No	No	No	Yes	No	134/84	No		X-ray showed calcification of pericardium; died in 1931, 3 months after last visit, probably coronary disease
8 C. R. R.	50 M	W	Cough Dyspnea	1 yr.	No	Yes	Yes	Yes	?	100/78	Yes	No	Condition very poor at present, 4 months following discharge
9 M. T.	48 M	C	Swelling abdomen	5 wk.	Yes	Yes	?	Yes	Yes ?	140/85	Ascites	No	Tuberculous peritonitis demonstrated; died 4 years after leaving hospital

TABLE IV—CONT'D

PATIENT	AGE SEX	COLOR	CHIEF COMPLAINTS	DURATION ILLNESS	PAST HISTORY TUBERCULOSIS	PERICARDIAL FRICTION RUB	VENOUS DISTENTION	ENLARGED SHADOW X-RAY	PARADOXIC PULSE	B. P. MM. HG	ASCITES PLEURAL EFFUSION ENLARGED LIVER	PERICARDIAL TAP	REMARKS
10 E. W.	21 M	C	Dyspnea Edema	1 yr.	No	No	?	Yes	?	104/66	Ascites	No	Tuberculous adenitis neck; died 6 weeks after leaving hospital
11 L. W.	57 M	C	Pain chest	3 mo.	Yes	Yes	Yes 70	Yes	No	94/58	Effusion Large liver	No	At present, 4 years later, partially incapacitated; pleurisy with effusion
12 F. W.	19 M	C	Pain chest	2 mo.	No	Yes	No	Yes	No	110/60	No	No	In hospital 12 days, improved on discharge; seen 7 years later, no evidence of pericarditis
13 W.W.W.	50 M	W	Dyspnea Edema	4 mo.	No	No	Yes 246	Yes	Yes	130/92	Yes	No	Incapacity continued; died 2 years after leaving hospital
14 H. W.	25 M	W	Pain chest	2 wk.	No	No	?	Yes	No	98/52	Effusion	No	At present, 6 years later, working regularly; no disability
15 L. C.	34 F	W	Dyspnea	3 yr.	No	No	Yes 250	No	Yes	98/74	Yes	No	Operation attempted; bleeding encountered; operation interrupted; definite constrictive pericarditis; etiology (?); died pneumonia
16 R. T. Y.	42 M	W	Dyspnea Edema	26 yr.	?	No	Yes 240	No	No	120/80	Large liver	No	Has mild constrictive pericarditis; etiology (?); disability 30 per cent
17 E. H.	60 F	W	Fever Weakness	3 wk.	Doubtful	Yes	No	Yes	No	105/50	No	No	In hospital 9 days, fever disappeared; 9 months since discharge, no symptoms
18 C. P.	43 M	C	Swelling abdomen	2 yr.	No	No	Yes 220	Slight	Yes	100/80	Ascites Large liver	No	X-ray shows mediastinal mass and calcification of pericardium; patient completely disabled at present, refuses operation

the anterior mediastinum or from those found at the point of reflection of the pericardium."

When the tuberculous infection reaches the pericardium by way of the blood stream, there is apt to be an associated miliary tuberculosis. Death usually ensues before the tuberculous pericarditis has progressed greatly. Pericarditis as a result of direct extension of infection from a neighboring focus is probably quite uncommon. Bellet, McMillan, and Gouley[7] state: "When the infection extends to the pericardium directly from a surrounding tuberculous lung, one may fail to see the usual gradual insidious development of the condition in which different stages of the process can be recognized. The condition may come on very suddenly and reach its maximum development very quickly; this is particularly apt to be the case when some contiguous tuberculous lesion ulcerates through the pericardium and pours into it its infected contents." It seems very likely that most instances of pericarditis are due to an extension of the infection through lymphatic channels from a mediastinal focus. The extremely high incidence of tuberculosis of the mediastinal glands in our patients supports this viewpoint.

A great deal has been written about "anatomically primary tuberculous pericarditis" and "clinically primary tuberculous pericarditis." The lack of a universally accepted definition for these two terms has resulted in confusion. In common with many others, we doubt the existence of an anatomically primary tuberculous pericarditis. Another focus of infection was demonstrated in all of our patients, with one exception, who came to autopsy. It is likely that a more careful search would have revealed a focus in this patient. Riesman[6] designated the clinically primary type as that in which tuberculous lesions elsewhere in the body could not be demonstrated at the onset of symptoms. Clarke[8] in 1929 stated that a careful search of the literature revealed only 11 such cases in which the diagnosis was unquestioned and he added 2 cases of his own. Some have broadened the term to include all cases of pericarditis unaccompanied by pulmonary tuberculosis. Thompson[9] states that primary tuberculous pericarditis usually occurs in elderly individuals. Roubier and Dubois[10] found 5 cases of primary tuberculosis of the pericardium without other tuberculous lesions in 1,300 autopsies. The youngest of these patients was sixty-seven years of age. In this connection, it is of interest in our patients in whom the pericarditis was the most important factor in the production of the clinical picture that most of them were more than forty years of age.

There seems to be a difference of opinion as to the part played by tuberculosis in the production of chronic constrictive pericarditis. Wells[11] found adherent pericarditis of various degrees in 57 of 1,048 autopsies. Six of these were frankly tuberculous and 43 were of undetermined cause. He stated: "By the above process of exclusion it has been attempted to show that many cases of adherent pericardium are

probably of tuberculous origin, although not showing any anatomic characteristics of tuberculosis. However, it is to be understood that this is not the only cause." Lilienthal[12] stated: "Few, if any, of the calcifications of the pericardium are of tuberculous origin." Sprague, Burch, and White[13] stated that tuberculosis of the insidious type is the most probable cause of the constricting pericarditis of Pick. Schur[14] reported 17 patients with adhesive pericarditis, most of whom had mediastinopericarditis rather than the constrictive type. Tuberculosis was believed to be the etiologic agent in 5 of these, but this was not proved. Tuberculosis was not demonstrated in any of the 7 patients upon whom pericardiectomy was performed by Beck[15] and reported in 1934. A recent personal communication states that he has performed a total of 20 operations for chronic cardiac compression due to pericardial scar and that 2 of these showed an active tuberculous infection. Rothstein[16] found in the literature the reports of 11 instances in which pericardiectomy had been performed on children. Tuberculosis was believed to have been the etiologic agent in 4 of these. White[17] had the following to say concerning the etiology of 15 cases of constrictive pericarditis which he and Churchill reported: "The etiology of the chronic pericardial disease can be assigned as follows: tuberculosis in two (questionable in two others), pneumonia with polyserositis (including both pleuritis and pericarditis) in two, sepsis in one, rheumatism in none, uncertain or unknown in 10 (in five of which, however, there was a definite history of acute pericarditis)." Of the 19 patients with undoubted constrictive pericarditis which have been studied in the Vanderbilt Hospital, 11 were proved to be tuberculous in origin and 5 others were believed to be. Our experience and particularly that of White, in Boston, makes one wonder seriously if rheumatic infection ever results in marked chronic constrictive pericarditis.

PATHOLOGY

The course of the typical case of tuberculous pericarditis may be divided into three stages. These are: (1) the acute fibrinous stage, (2) that in which there is an effusion and moderate thickening of the pericardial surfaces, and (3) the stage in which most or all of the effusion disappears and the pericardium and epicardium become greatly thickened. In some cases, still another stage appears in which the active tuberculous infection completely heals and only a thick dense scar remains. In most cases, there is a long-continued infection and the condition found at autopsy or operation depends in the main on the severity and the duration of the disease. We shall not attempt to describe in detail the various stages of the disease which may be encountered. Osler[1] stated: "The membranes may reach a thickness of from three to 10 millimeters, the increase being due to the growth in the leaves of tubercles, the development of caseous masses, and to the new growth of

connective tissues. Frequently it can be seen that the two enormously thickened layers are united by a clear, infiltrated tissue, which may itself not present any tubercles. In the earlier stages of this process the membranes are little, if at all, thickened, the tubercles are seen just beneath the endothelial layer, and there may or may not be a fresh exudate of yellowish fibrin. In other instances, the contiguous surfaces of the thickened layers are covered with flat, yellowish caseous masses. Collections of thick cheesy pus are occasionally found between the layers."

Pericarditis due to other causes, rheumatic fever in particular, is more apt to disappear rapidly or to pass quickly to the adhesive stages. There is usually a long-continued chronic infection in tuberculosis, and it is likely that this disease accounts for the majority of the cases of chronic constrictive pericarditis.

TREATMENT AND PROGNOSIS

The treatment of tuberculous pericarditis in the acute fibrinous stage consists in the employment of rest in bed and of narcotics for the relief of pain. If and when an effusion develops, it is probably advisable not to perform frequent aspirations except for the purposes of relieving dyspnea and evidences of marked systemic congestion. It is believed by some that aspiration of fluid followed by replacement with air is of benefit. Everyone is agreed that the pericardium should not be drained during the stage in which an acute effusion is present. When the tuberculous process becomes entirely inactive and evidences of compression of the heart persist, everyone is agreed that the scar should be removed. There is some difference of opinion as to the treatment to be employed when the patient's condition is becoming worse and the venous pressure is rising despite the fact that the heart-pericardial shadow has decreased in size. It is our impression that operation should be undertaken at this time even though the infection is believed to be active. In this regard, Churchill[18] states: "Active tuberculosis of the pericardium may produce the entire syndrome of chronic constrictive pericarditis. The point at issue is whether operation can be effective if performed during the active stage of the infection. The reports in the literature of operations performed during this period are uniformly discouraging and confirm our personal experience." Beck[19] stated recently: "As long as the tuberculosis shows activity, one cannot expect to relieve the cardiac compression."

Two of the patients in Churchill's series had an active tuberculous pericarditis at the time of operation. In regard to these, he stated:[18] "Both patients died promptly, one on the operating table and the other a few hours subsequently, their lives being shortened a few days as a result of the operative procedure." In considering our 6 patients with proved tuberculous pericarditis with activity on whom pericardiectomy

was performed, it is to be observed that 1 of the 3 deaths occurred immediately following the operation. This death might have occurred irrespective of the question of activity of the infection and may be ascribed to an error in operative technique or to the poor condition of the patient. The other 2 deaths occurred two and six months respectively following the operations. Both of these patients were improved temporarily but developed miliary tuberculosis subsequently. It would appear to be doubtful if the operation hastened the fatal outcome. The remaining 3 patients are much improved following decortication of the heart.

We shall not consider in detail the operative technique for the removal of the pericardial scar. Excellent descriptions have been supplied by

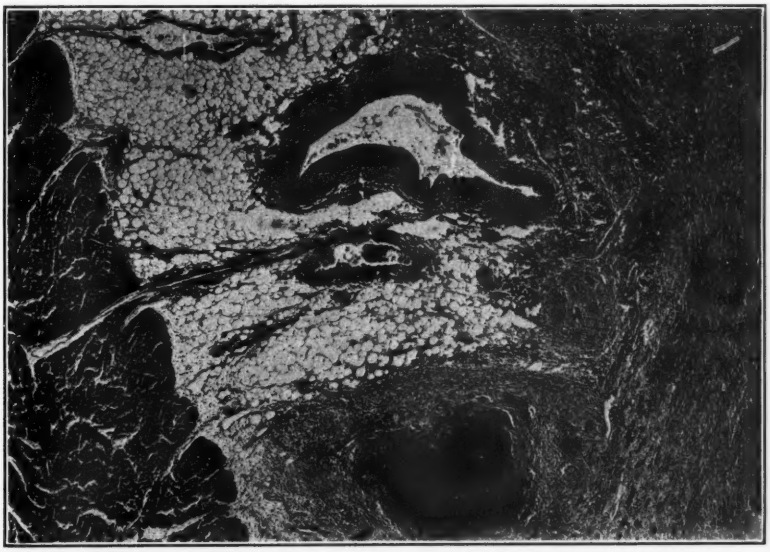

Fig. 1.—Section (×40) of autopsy specimen (Case 3, Group II) showing scar and heart muscle, with coronary artery intimately attached to the scar.

Schmieden,[20] Churchill,[18] Bigger,[21] and others. Needless to say, it helps little, if at all, to remove a pericardial scar if another scar corresponding to the epicardium is left behind. On the other hand, one should be extremely careful not to include the coronary vessels with the scar that is removed. In some instances, the vessels are more intimately attached to the scar than to the heart muscle. This is illustrated by a photomicrograph of an autopsy specimen which is shown in Fig. 1. The death of one of our patients (Case 5, Group I) may have resulted from this error in operative technique. In this regard, Churchill[18] states: "The sulcus formed by the descending branch of the left coronary artery is apt to be the site of densely adherent scar, and this region should be approached with caution to insure the preservation of this important

vessel. . . . A maneuver that has been advantageous in several instances has been to establish a new plane of cleavage over the right ventricle so that the inter-ventricular groove may be approached from both sides.''

As has been stated, Harvey and Whitehill[5] reported 17 patients with tuberculous constrictive pericarditis without effusion, and 15 of the 17 died. It is not stated what happened to the remaining 2 patients. Pericardiectomy was not performed on any of these. In our series, all patients on whom a positive diagnosis of tuberculous pericarditis was made are dead with the exception of the 3 on whom pericardiectomy was performed and another patient who is completely disabled in the hospital at the present time. We do not mean to imply that all patients with tuberculous pericarditis die unless a decortication of the heart is performed. Certainly a number of the patients in the group in which tuberculous pericarditis was suspected but not proved had the disease and some of them are well. It seems likely that they had a less fulminating type of infection or that their resistance was greater. Also the fact that some of the healed pericardial scars which have been reported were almost certainly tuberculous in origin is evidence that the acute infection is not always fatal. On the other hand, pericardiectomy would seem to be indicated in those individuals who grow worse rather than better as the effusion disappears.

SUMMARY

In summary, 42 patients in whom tuberculosis of the pericardium has been strongly suspected or proved have been admitted to the Vanderbilt Hospital during the past eleven years. Eighty-six per cent of the patients were males and most of those in whom the pericarditis constituted the chief cause of the illness were forty or more years of age. A positive diagnosis was made as a result of aspiration, operation, or autopsy in 24 cases. Only 4 of these 24 patients are living at present. Pericardiectomy was performed on 3 of the 4 and they are doing quite satisfactorily. The remaining patient has a subacute tuberculous pericarditis and is quite ill. Tuberculous pericarditis was strongly suspected but not proved in 18 cases, who in general were less ill than the others. Eight of these patients are dead and 4 are free of symptoms, and the others are wholly or partially incapacitated. The incidence, etiology, pathology, treatment, and prognosis of the disease are considered.

It is a pleasure to express our thanks to Dr. C. S. Burwell and Dr. E. W. Goodpasture.

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DISCUSSION

DR. I. A. BIGGER, Richmond, Va.—I would like to congratulate Dr. Blalock on his extremely interesting paper.

In this connection I think it may be of interest to discuss briefly a patient whom we operated upon last year for a tuberculous pericarditis with a secondary streptococcus infection. After repeatedly demonstrating streptococci in the fluid aspirated from the pericardium, we did a pericardiostomy and at the same time removed a small section of the pericardium for microscopic examination. This showed an active tuberculous infection as well as a secondary pyogenic infection. The pericardial cavity contained approximately 1,000 c.c. of purulent fluid at the time of the first operation.

The pericardium continued to drain over a period of several weeks, but during this time the right side of the cavity was slowly obliterated, leaving a persistent cavity on the left side. He was given x-ray therapy over the anterior pericardial area. Three months after the pericardiostomy and five weeks after the x-ray treatment, the patient developed evidence of a constricting pericarditis and a partial pericardiectomy was done. The portion of pericardium removed was studied carefully and no evidence of active tuberculous infection was found. This was of considerable interest to me, for while the tuberculosis of the pericardium may have healed spontaneously, it seemed likely that the irradiation played a part in the healing.

DR. C. S. BECK, Cleveland, O.—I believe that Dr. Blalock has made an important addition to the knowledge of tuberculous pericarditis and its treatment.

Recently I was forced to operate upon a patient who had compression of the heart, which was getting worse, and which we thought was due to tuberculosis. Fluid was being tapped from this patient's chest every three days. He had a marked degree

of ascites, and he was losing ground. Reluctantly I operated upon him and took off a very thick pad of pericardial scar. The patient showed improvement after the operation for a few weeks, and then lost what improvement he had made. Gradually over the course of a few months he had begun again to show improvement.

Personally, I feel that if the patient can go along without operation on medical treatment, perhaps the wisest thing to do is to let him go along until the activity of the infection subsides. I have one such patient now who has active tuberculosis in the pericardium and who is being given medical treatment in the hope that the activity will subside. I also had one patient who had tuberculous effusion in the pericardium and a typical picture of compression of the heart. This patient has received a cure from repeated aspirations of the fluid from the pericardium without open operation.

DR. EDWARD D. CHURCHILL, Boston, Mass.—A recent operative observation throws light on the pathogenesis of at least one case. A man who had had tuberculous peritonitis in early life was operated upon to remove a constricting pericardium. In striking a plane of cleavage over the left phrenic nerve, the adhesions were observed to grow more dense and appeared slightly edematous. Realizing I was approaching an abscess, the dissection was continued cautiously until an extrapericardial tuberculous abscess containing an ounce of pus was opened. The abscess was anatomically situated external to the pericardium but perforating into it.

So in this particular patient a suppurating tuberculous mediastinal lymph node had at one time perforated into the pericardium and set up a transient tuberculous effusion which had healed; or possibly, the lymph node abscess had by contiguity caused a pericardial reaction resulting in scar.

The suggestion that the origin of certain cases of the Pick syndrome may be due to extrapericardial tuberculosis of the lymphatic system is substantiated.

I am delighted that Dr. Blalock gives us more courage about active tuberculous pericarditis. I have always felt that these cases should be operated upon because in many instances we are unable to tell clinically whether the process is active or healed. The removal of one rib under novocaine will reveal very readily what one may hope to accomplish. Of course in dealing with any active case of tuberculosis, even if thick pus is encountered, silk technique and closure without drainage is very important. Even then a sinus may develop in the scar months later.

DR. HUGH TROUT, Roanoke, Va.—Many more years ago than I like to admit, I was a student under Dr. Pick. Ever since that time I have naturally been interested in adherent pericarditis and in watching the development of the various theories as regards the etiology. Due to our interest in the disease, we have been able to pick up more cases than we would have otherwise.

We have operated upon 5 cases, and 2 of them died almost on the operating table, and the other 3 had fairly good results, the best result being the one case that is now alive over five years.

For many years the impression was that the chief etiologic feature to the disease was acute inflammatory rheumatism of childhood. In recent years, however, the indications are more and more definite that tuberculosis plays a far more important part in such a rôle. In recent years we have been able to see quite a few cases which showed, by the use of the fluoroscope, that there was a conflict between the pericardium and the diaphragm. These cases are usually classified as mediastino-pericardial adhesions, and relieved by the Brauer type of operation. Frequently the interruption of the phrenic nerve produces marked benefit. Not only is there marked clinical improvement after such a simple procedure, but the examination with the fluoroscope shows the cessation of the conflict between the pericardium and the diaphragm.

In the last three cases of cardiolysis we found this procedure of marked benefit as a preliminary step in operation. The phrenic interruption was done about

two weeks before operation and the patient's condition improved. Naturally, if the x-ray shows the heart to be small and encased in a leatherlike pericardium, interruption of the phrenic would be of no value.

Our attention was called to the possibilities of benefits resulting from this simple procedure by the following observation: When we interrupted the phrenic nerve on the left side in basal lesions, there was more marked improvement in pulse both in rate and volume than there was when we interrupted the nerve on the right side.

DR. JOHN W. STRIEDER, Boston, Mass.—In connection with the excellent papers that Dr. Blalock, Dr. Beck, and Dr. Stephens presented on cardiac surgery, I should like to be permitted to recount very briefly a somewhat different experience which we had with an operation which, as far as we know, had never before been attempted; namely, the attempt of obliteration of a patent ductus arteriosus in a patient who already had subacute bacterial endarteritis. I should also be very gratified to be corrected if there is a record of a similar experience before.

To go back for just a moment, we had had some interest in this particular operation as a prophylactic measure in patients with patent ductus arteriosus, and carried out a series of dissections in the dissecting room as a preparation to attempting it in the living. Dr. Reginald Fitz, however, called to our attention a patient who was referred to him with a patent ductus arteriosus who had had subacute bacterial endarteritis.

I might say, without going into detail, that the approach was through a modified Delorme incision with removal of the second and third cartilages and retraction of the left pleural sac outward. The operation was extremely easy, down to the point of exposing the patent ductus, the fibrous pericardium, and the roots of the great vessels. The patent ductus in this particular case was made up of a contiguity of the two walls of the aorta and pulmonary artery. Although it was possible to free this fusion laterally, mesially, and anteriorly, posteriorly it was so closely in relation to the right branch of the pulmonary artery that we didn't feel it advisable to attempt to pass even a single ligature for temporary relief. At all events, an attempt was made to plicate, and a series of silk sutures were placed and there was almost complete diminution of the palpable thrill.

The patient was in an extremely precarious condition when the operation was begun with a pulse of 160 and respiration of 60. She made an excellent postoperative recovery for four days. On the third day, the murmur was no longer heard, but she died on the fourth day of an acute dilatation of the stomach. At autopsy the findings at operation were confirmed, but, in addition, it was found that the vegetations had extended from the orifice of the patent ductus down to the pulmonary valves. I may say that, preoperatively, there were no peripheral manifestations of emboli. There were manifestations of pulmonary emboli, and in that connection it was thought the operation was worth trying if there was anything to be gained at all.

We are reporting this in some detail later, but I thought I might take the opportunity to present it to the Society in case anyone had thought along similar lines and would be interested in trying it as a prophylactic measure in youngsters before they already have dilatation and hypertrophy of the heart, and also because 25 per cent of these congenital heart defects die of subacute bacterial endocarditis or endarteritis.

I would also like to say that Dr. Donald Munro, of Boston, whose father, Dr. John Munro, was formerly chief of the Boston City Hospital, told me personally that he thought his father had attempted the operation, unsuccessfully, some forty-five years ago. We were unable to find any record of it in the records at the Hospital, but later found that he had proposed the operation in 1907 before the Philadelphia

Academy of Surgery. He had carried out dissections on the bodies of newborn infants, in a somewhat different manner, but he had never attempted it in the living.

DR. WM. F. RIENHOFF, Baltimore, Md.—I have been very much interested in Dr. Blalock's excellent paper, and I want to ask him two questions. We have only had a few cases of constrictive pericarditis, and in one of them, tuberculous pericarditis, although proved at operation, was unsuspected before. The patient presented the typical signs and symptoms of ascites, with enlargement of the liver, poor pulse volume, small heart, and required frequent abdominal tappings. The venous pressure ran between 245 and 270 while in bed. The patient was a very ill man of sixty-five years. The chart revealed a low-grade elevation of temperature. The question as to whether or not he might have tuberculous pericarditis was discussed by Dr. Longcope but was never proved. Pericardiectomy was performed by me in the usual manner, and after operation the patient went back to the medical service where he remained for four months before there was any improvement at all. Then, his venous pressure slowly returned to normal, the tappings which for four months after operation were almost as necessary as before, ceased to be necessary, no more fluid accumulated in his chest, and he is now up and around and perfectly well. Tuberculosis wasn't suspected until the report came back from the pathologic laboratory.

The question came up in the staff meeting regarding this patient, how could the correct diagnosis have been made, and if it had been made, with a low-grade elevation of temperature before operation, running up to 99° and 99.6° each day, would it have been advisable to have operated upon him at that time, or would it have been better to allow him to rest? Also, why did it take so long for him to reestablish his circulatory balance? These were questions that we were unable to answer. I would like Dr. Blalock to throw some light on them and answer them in the light of his large experience.

DR. H. C. BALLON, Montreal, Canada.—May I refer Dr. Strieder to the publication of J. C. Munro entitled "Ligation of the Ductus Arteriosus" (Ann. Surg. 46: 335, 1907) and referred to by M. E. Abbott in her book on *Congenital Cardiac Disease* (Philadelphia, 1927, Lea and Febiger). Reference has also been made to this subject by Graham, Singer, and Ballon, in *Surgical Diseases of the Chest* (Philadelphia, 1935, Lea and Febiger).

DR. ALFRED BLALOCK, Nashville, Tenn. (closing).—I can't answer Dr. Rienhoff's questions, I am sorry to say. His experience is similar to ours in that it frequently takes these patients a long time to improve. We had a patient who required a year for his venous pressure to decline to the normal level and for the output of the heart to increase to a normal level.

Most of the signs and symptoms in this disease are due almost certainly to the increased venous pressure. There have been several patients following operation who had a decided improvement with a drop in the venous pressure, with very little increase in the output of the heart, the increase in the output of the heart coming subsequently.

As to how one tells when a patient should be operated upon, I can only say that if a patient is getting worse despite the fact that the heart pericardial shadow is decreasing in size, if the venous pressure continues to rise with this decrease in size, we think the patient should be operated upon, because otherwise he will almost certainly die.

We agree entirely with Dr. Beck in regard to his statements, and I simply wish to emphasize again that we do not think that every patient with an active tuberculous pericarditis, even when most of the fluid has disappeared, should be operated upon, but that one should operate when it looks as though the patient is going to die if something isn't done.

CHEMOTHERAPY IN THE TREATMENT OF STREPTOCOCCUS INFECTIONS OF THE LUNG PLEURA AND CHEST WALL*

(PRONTOSIL AND PRONTYLIN)

HARRY C. BALLON, M.D., AND ALTON GOLDBLOOM, M.D.
MONTREAL, CANADA

IT IS chiefly because of the exhaustive researches of Colebrook and his associates and their carefully controlled clinical tests that prontosil and prontylin have come to be so widely used in disease due to the hemolytic streptococcus. We wish to report here some of our experiences with these agents in the treatment of infections of the lung, pleura, and chest wall caused by the hemolytic streptococcus.

Since our observations concern a limited number of cases, we have purposely refrained from drawing any conclusions. A striking result may justly be regarded by some as mere coincidence, by others as a tendency to spontaneous cure of the infection. Our first case is deserving of special consideration. Personal experiences with this form of therapy have not been confined to the type of cases reported here in detail.

Although Domagk in 1935 first demonstrated that prontosil exerts a selective action upon streptococcus infection in mice, the results obtained left much to be desired. Levaditi and Vaisman, using a similar compound synthesized by Gerard, obtained somewhat similar results, while Nitti and Bovet were unable to confirm Domagk's results in experimental septicemia. Colebrook and Kenny also failed to confirm Domagk's claim in its entirety, but were able to demonstrate curative effects of the drug in mice. Certainly Colebrook and his associates have shown that prontosil has little, if any, "bacteriostatic" action. Long and Bliss confirmed this observation by demonstrating that dilutions of "prontosil solution" had no effect on the growth of beta-hemolytic streptococci in 0.075 per cent dextrose beef-infusion broth, or in fifty per cent normal horse serum broth. When various concentrations of para-amino-benzene-sulfonamide were used, a marked reduction in the growth of the streptococci was observed. It is worthy of repetition that Long and Bliss reported that mice have died of streptococcic infection as late as seventy-four days after the infection, or sixty days after treatment with "prontosil solution" had been discontinued. During the interval the mice are said to have enjoyed good health.

Apparently prontosil must be altered in the body before it can become active. It has been shown that the serum of animals previously injected

*From the Departments of Surgery and Pediatrics, Jewish General Hospital, Montreal.

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with prontosil has marked "bacteriostatic activity." Further it has been suggested by Fuller and by Long and Bliss that prontosil becomes converted into sulfanilamide which is probably the active principle. Fuller found that in human beings para-amino-benzene-sulfonamide is excreted in the urine in both free and conjugated forms. Marshall, Emerson, Kendall, and Babbitt state that the drug is excreted in dog's urine unchanged; in the case of the rabbit large amounts are excreted in conjugated form. Absorption from the gastrointestinal tract appears to be rapid, being complete or nearly complete in about four hours. Where large doses are given in daily divided doses, nearly 100 per cent may be recovered from the urine when equilibrium between intake and output is established. "It takes from two to three days to establish this equilibrium, and the same time to free the body of the drug after it is discontinued." These investigators have also observed that sulfonamide appears to be excreted more slowly in patients with impaired renal function. Southworth has drawn attention to the fact that acidosis might result from the use of these agents; Colebrook and Kenny, and more recently, Discombe, referred to the occurrence of cyanosis associated with sulphemoglobinemia.

We observed mild reactions on three occasions. One was manifested by abdominal pain and headache, another by frequent bowel movements, and the third by fever and headache. For practical purposes the individual who suffered the latter reaction may be regarded as normal.

Cooper, Gross, and others referred to elsewhere have reported on the effect of these drugs upon Type III pneumococcus infections in mice. Schwentker and his coworkers have reported upon their use in the treatment of beta-hemolytic streptococcal meningitis. Their clinical results to date have been gratifying.

Few published clinical reports, which are numerous and have been repeatedly referred to by others, give detailed descriptions of the clinical condition and of the severity of the infection. We have, therefore, chosen to report some of our cases in detail. The question of dosage will be considered in the discussion.

CASE REPORTS

CASE 1.—R. B., a female, aged eleven years, was found to be suffering from a mild scarlet fever on June 17, 1935. A few days later she developed a left-sided otitis media. This necessitated the performance of a myringotomy on which occasion pus was obtained. The discharge, however, did not persist for long. A second complication, namely, bilateral cervical adenitis made its appearance one week later. Fever persisted and at times the patient also complained of pain over the cervical spine, and of dysphagia. The presence of a retropharyngeal abscess could not be established either clinically or roentgenologically. During the fifth week of her illness, it became necessary to incise and drain the cervical glands on the left side. The enlarged cervical glands on the right side had returned to their normal size. The glands on the left side of the neck were again incised two weeks later; this time at a different site, but no pus was obtained. She then received scarlet fever

antitoxin which provoked a serum reaction. Again it became necessary to incise an abscess on the left side of the neck. The incision in this instance was not made at the original site.

When the patient first came under our observation on Nov. 6, 1935, her complaints were discharging sinuses of the neck, inability to straighten her head, fever 99° to 101°, anorexia, and cough. There were, in addition, loss of weight and strength. The actual weight loss was 10 pounds. Her weight at this time was 109 pounds. She was free from expectoration or dysphagia. Both sides of the neck, particularly the left, showed multiple ulcers and sinuses which were discharging pus. They were spread over the neck in a veritable collar fashion and were filled with listless granulation tissue. On either side they were situated about an inch above the level of the clavicles, in the midline extending down to the jugulum, and on the left side extending upward behind the sternomastoid muscle for a distance of 2½ inches. In places the skin about the ulcers showed undermined edges. There was but slight tendency

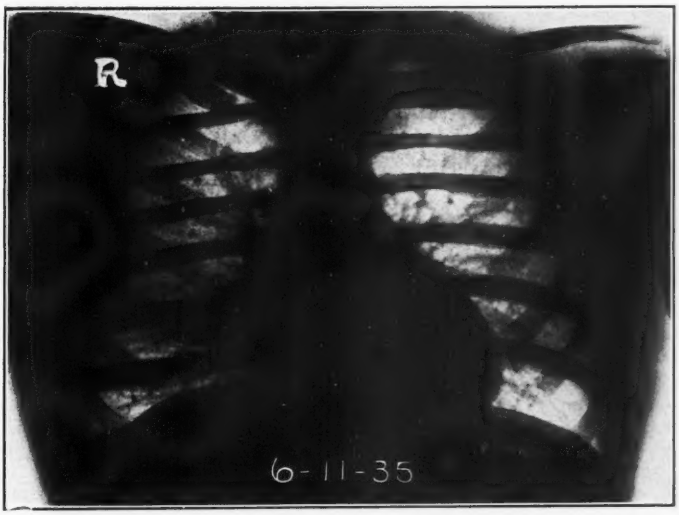

Fig. 1.—(Nov. 6, 1935.) Save for a few areas of calcification, both lung fields are clear. Note the interlobar fissure, right. Both diaphragms occupy their normal positions; there are no skeletal changes. The onset of this patient's illness was on June 17, 1935.

to rolled-in margins. To the right of the sternum an ulcer, the size of a fifty-cent piece, was separated by a small bridge of healthy skin from a smaller ulcer situated at the level of the jugulum. None of the openings in the skin would permit the introduction of a probe for any great distance. There were no palpable glands, locally or generally. The head was drawn acutely over to the left side, and it was impossible to straighten it. At first glance the entire picture suggested tuberculosis or actinomycosis. In this connection it may be noted that there was no history of exposure and that the patient's personal and family histories contained nothing worthy of note.

She was admitted to the Jewish General Hospital on Nov. 6, 1935. A direct smear of the discharge from the sinuses revealed cocci. There were no acid-fast bacilli nor was there any evidence of actinomycosis. The blood Wassermann reaction was negative; the urine clear. The blood picture showed 4,500,000 r. b. c., hemoglobin 85 per cent, w. b. c. 27,100. The differential blood picture revealed a slight degree

of normochromic microcytic anemia, anisocytosis and poikilocytosis, markedly increased sedimentation rate, slight reticulocytosis, marked leucocytosis with marked neutrophilia, marked lymphocytosis and slight monocytosis, some toxic granules in the neutrophilic cytoplasm, and marked shift of the polynuclears towards immature forms.

Roentgen ray examination of the cervical spine on Nov. 7, 1935, again failed to show any variation from the normal. Examination of the chest (Fig. 1) revealed increased hilum detail which was not regarded as tuberculous in origin, although the child gave a strongly positive response to a Mantoux test 1:1000.

A diagnosis of suppurative tuberculous cervical adenitis with multiple sinuses was made at this time. Dr. Bazin, who also saw the patient on this occasion, concurred with this diagnosis. It was agreed that, in addition to the usual regime, ultraviolet radiation and roentgen ray therapy were indicated; further, that better results would be obtained if the sinuses were first freshened and prepared for radiation therapy. This was done accordingly under ethylene oxygen anesthesia on Nov. 12, 1935.

All sinuses and undermined edges were laid open. This did not call for any extensive procedure for everywhere the tissue underlying the grayish gelatinous material, which was wiped away, was dense, extremely hard, and fixed. On the left side there was a tract which led down to the carotid vessels. The left sternomastoid muscle was fixed. There were no broken down or enlarged glands in the field of operation. It was originally intended to cauterize the wound, but there seemed no justification for this procedure at the time of operation. When the operation was completed, a healthy base seemed to have been prepared everywhere. Two iodoform packs were placed loosely in the wound. Specimens, which consisted of many tiny bits of gray semifluid material and several large pieces of firm gray tissue, measuring up to 1 by 0.5 by 0.2 cm., were sent to the laboratory for microscopic examination and were reported upon by Dr. Seecof as follows:

"Several bits of tissue are made up of necrotizing granulation tissue in which are many newly formed thickened capillaries and occasional chronic granuloma giant cells. Some sections show infiltration of fat by the necrotizing granulation; others show granulation tissue covered by layers of stratified squamous epithelium showing hypertrophy of the papillae. Within the corium are localized accumulations of giant cells, in addition to leucocytic and plasma cell infiltration. Gram and acid-fast stains reveal no organisms. Diagnosis: chronic granuloma, etiology undetermined."

The immediate postoperative course was stormy. The simple surgical procedure which had lasted but twenty minutes in this case, provoked an alarming reaction as did all subsequent ones, even though minor in nature. The patient's temperature rose to 106°, dropping to 100° in thirty-six hours. There was no definite evidence of pulmonary atelectasis, so that much of the reaction was attributed to the handling of infected granulation tissue rather than to temporary septicemia. The patient was discharged from the hospital on Nov. 21, 1935, against advice. Her temperature curve now showed a daily elevation of 2°. For a time the ulcers were covered by liquid paraffin dressings, then irrigated with normal saline, and later with Dakin's solution. The dressings had to be changed at frequent intervals because of the copious discharge.

Ultraviolet radiation, which was given a fair trial, increased the temperature reaction but did not lessen the discharge, and increased local pain and several times made her feel quite ill. On these occasions herpes labialis was noted. She was then made to rest more, was placed on forced feedings, and received iron tonics, vitamins, and considerable potassium iodide.

She was then started on an intensive course of x-ray therapy by Dr. Liebman, and for a short time only, we regarded her condition as slightly improved. She returned

to Halifax, where x-ray therapy was continued. On Dec. 27 her father reported that he believed there was some change for the better in the condition of his child's neck. He brought her back, and she was readmitted to the hospital on Jan. 6, 1936. On this occasion she remained in the hospital until June 14, 1936. At this time we were not impressed by the local or general improvement in the child's condition, following the treatment to date. The ulcers and sinuses were deeper and wider. Here and there the edges showed an abundance of granulation tissue, elsewhere one observed grayish green jellylike tissue. The course of x-ray therapy was completed. All to no avail! Dr. Goldblatt, of Western Reserve University, then provided us with phenyl mercury borate tincture, which we employed on dressings and as an irrigation. We were unable to employ it in the recommended dilutions, namely, one part to nine of distilled water. We were forced to content ourselves with dilutions of one in fifty. As was the case with other irrigations, the child would not permit them to be carried out satisfactorily, because they increased her pain and made the surrounding skin tender. They did not reduce the amount of discharge nor did they improve the general appearance of the local condition. We then resorted to cod liver oil ointment, next to hydrogen peroxide, and then to hot moist boracic dressings. The latter at least caused no pain. Early in February she contracted German measles, and we were soon back where we had started many months before.

We soon decided to attempt to correct the patient's torticollis in order to promote more adequate drainage. This was accomplished rather satisfactorily by Dr. Goldman, who employed traction by means of a neck halter. The head of the bed was elevated. Starting with a one-pound weight, traction was adjusted so that the pull was directly to the right side. Within two weeks it was possible to increase the weights to ten pounds, and the patient now held her head much straighter. For some time we had not been satisfied with the diagnosis, let alone with the treatment. On March 10, 1936, Dr. Usher saw the patient and suggested that the condition was scrofuloderma. A Frei test done about this time was negative.

The patient was seen by Dr. Cushing on April 25, 1936. He regarded the condition as one of the rarer complications of scarlet fever, and stated that he had observed two or three much milder cases during the past twenty years at the Alexandria Hospital for contagious diseases. They were apparently observed in children, with negative tuberculin reactions. He demonstrated one such case to us at the time.

During April it was noted that pressure on the left trapezius and pectoral muscles permitted pus to be milked up through the sinuses, particularly the large one in the left neck. A roentgen ray film on April 6 showed some periosteal reaction about the left clavicle.

Roentgen ray examinations of the chest and sternum on the same date were reported by Dr. Liebman as follows: "Examination of the chest shows numerous calcified areas in both hilus regions, undoubtedly the result of healed tuberculosis. There are several small, calcified areas in the parenchyma of both lungs which are also indications of healed foci. There is no evidence of any involvement of the sternum and no definite sinus tracts can be seen."

On April 13 Dr. Seecof reported that smears of the purulent material from the sinuses showed gram-positive cocci, and were acid-fast negative. Guinea pigs inoculated with purulent material showed no evidence of tuberculous infection when killed. Cultures showed a mixture of hemolytic staphylococcus aureus and staphylococcus albus. No anaerobes were found.

She continued a downhill course during May, and early in June the temperature curve assumed an even more septic appearance. A blood culture at this time failed to show any growth. Over the left chest the percussion became impaired from the apex to the third rib anteriorly and fifth rib in the axilla. Breath sounds were diminished. There were no râles; the mediastinal contents were not displaced. The urine now showed a heavy trace of albumin, anemia was marked. Reexamination of

the chest on June 6 showed slight but definite clouding over the right apex. There appeared to be an oval-shaped area of increased density directly in the apex, but this appeared to be extrapulmonary. There was a definite irregularity of the distal end of the second rib and of the clavicle (Fig. 2). These changes were regarded as due to long-standing chronic irritation from without, since there was no evidence of bone destruction, but rather periosteal reaction and new bone formation.

The density over the apex of the lung was clinically regarded as due to a subpectoral abscess. Before undertaking drainage of this abscess, it was decided to attempt to build up the patient's resistance. Professor Murray, of the Department of Bacteriology of McGill University, had previously been consulted. The results of his findings may be summarized as follows: Pus collected from the sinuses on several occasions and cultured on a variety of media aerobically and anaerobically yielded pure growths of streptococcus hemolyticus. No staphylococci were present. Pus collected from a superficial pustule yielded a growth of two colony forms of a staphylococcus-like organism. It was Professor Murray's impression that the main infection seemed to be due to the streptococcus hemolyticus.

An autogenous F-S Vaccine was prepared (having 64 F-S hemolytic units per cubic centimeter). It was suggested that it be given at five-day intervals sub-

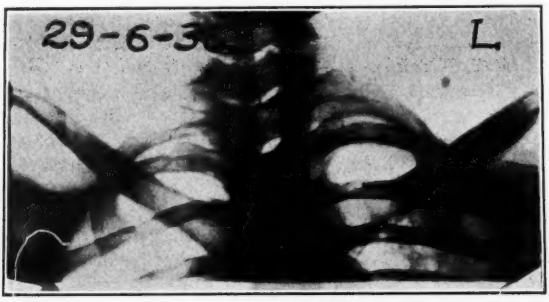

Fig. 2.—(June 29, 1936.) Note the changes in the terminal portion of the first rib and the periosteal reaction about the left clavicle. This film was taken one year after the onset of this patient's illness.

cutaneously in doses of 0.5 c.c., 0.1 c.c., 0.25 c.c., 0.75 c.c., and 1 c.c. The vaccine was given as recommended. During part of the treatment the child rested in the Laurentian Mountains, some sixty miles from Montreal. The injections provoked slight local but no general reactions.

On June 24, 1936, Professor Murray reported that special cultural examinations, aerobically and anaerobically and using concentration methods, failed to reveal the presence of any yeasts, molds, actinomycetes, or mycobacteria. In addition that no microorganisms, other than those described in previous reports, had been found. Cultures of another specimen gave a growth of streptococcus hemolyticus only.

Examination of the dorsal spine on June 29, 1936, showed no variation from the normal. Examination of the ribs showed a large area of destruction involving the anterior end of the first rib on the left side, suggesting osteomyelitis. The second rib on the same side also showed an area of destruction in its anterior portion.

The third admission to the hospital was on July 22, 1936. This became necessary because the subpectoral abscess, and the collection of pus under the left trapezius muscle high up now required drainage. The patient on this occasion looked quite ill. She showed further loss of weight. The only comforting feature of the case was the fact that the new abscesses were forming at lower levels, over the thoracic cage between the ribs and chest wall, and that they were not burrowing towards the mediastinum. Movement of the left shoulder was very limited and extremely painful.

This was attributed largely to the subpectoral abscess. Following a blood transfusion the abscesses were adequately and liberally incised and drained, the former after the method recommended by Lilienthal. In the case of the abscess under the trapezius muscles, counter drainage was established. Both abscess cavities were lined by very hard tissue. It was possible to palpate the underlying ribs anteriorly. They appeared very rough, but the findings suggested periostitis rather than osteomyelitis. The late Dr. Scrimger participated in this operation and agreed with the interpretation of the findings. The abscess cavities were packed loosely with vaseline gauze. A continuous intravenous clysis of glucose saline was maintained for a week postoperatively. The immediate postoperative course in every respect resembled that which followed the first operation. The temperature rose to 105°, dropping in forty-eight hours to 101°, and thereafter ranging from 99° to 102°. The pus obtained from the abscesses revealed streptococci and diplococci. Pus continued to drain everywhere.

Fig. 3.—(Sept. 24, 1936.) Note the density which starts in the left apex and which extends below the third rib anteriorly. The first four anterior ribs show changes, chiefly periostead. The density at this time was attributed to a collection of pus in the soft tissues of the chest wall.

The results of the drainage operations could hardly be called gratifying, or even encouraging, for neither the temperature curve, discharge from the sinuses, degree of anemia, nor leucocytosis, was beneficially influenced. On the contrary, soon all became worse. By now it was necessary to change the dressings every two or three hours; on all occasions they were soaked with pus. The preoperative blood count showed leucocytes 22,000. Four weeks later it showed no appreciable change, save that the degree of anemia was more marked. A roentgen ray examination of the chest on August 12, 1936, showed further destruction of the first and second ribs on the left side. The density noted in the region of the left apex of the lung was attributed to an accumulation in the soft tissue, not to an empyema.

On August 20, 1936, Professor Murray reported that, using the material collected on May 19, the cultural examinations and animal inoculations for the special purpose did not reveal the presence of either mycobacterium tuberculosis or pathogenic fungi.

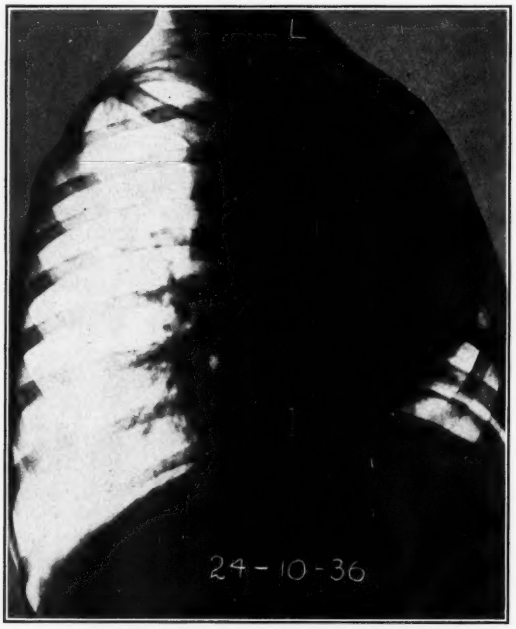

Fig. 4.—(Oct. 24, 1936.) The extreme density occupying the greater part of the left chest is due to inflammation and a collection of pus between the endothoracic fascia and the ribs, and partly to involvement of the chest wall and undersurface of the pectoral muscles and muscles of the back by a similar process. This fact was established at the time the subpectoral and posterior abscesses were drained. A film taken three weeks after the above showed even further extension of this process, both front and back, down to the level of the diaphragm.

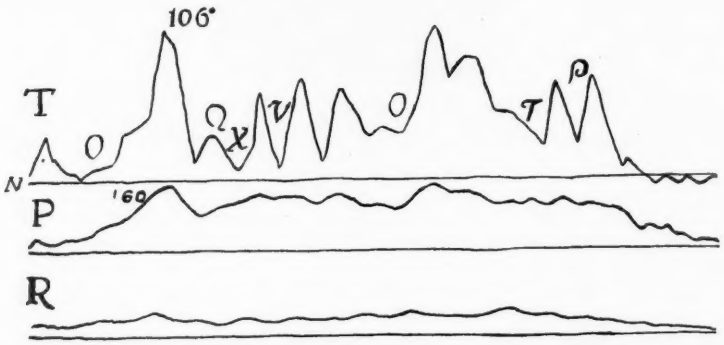

Fig. 5.—The pulse, temperature, and respiration curves clearly note the sharp and alarming reactions which followed simple surgical procedures (noted by *O*, operation); *Q*, denotes the type of temperature the patient was exhibiting when quartz light therapy was employed; *X*, when x-ray therapy was given; and *V*, when vaccine was given. The second letter *O* indicates the temperature reaction which followed the drainage of the subpectoral and posterior abscesses; *T*, the type of temperature curve when the blood transfusions were given. The temperature which previously showed daily elevations of 103° and 104° dropped to normal following the administration of prontylin and has remained so ever since.

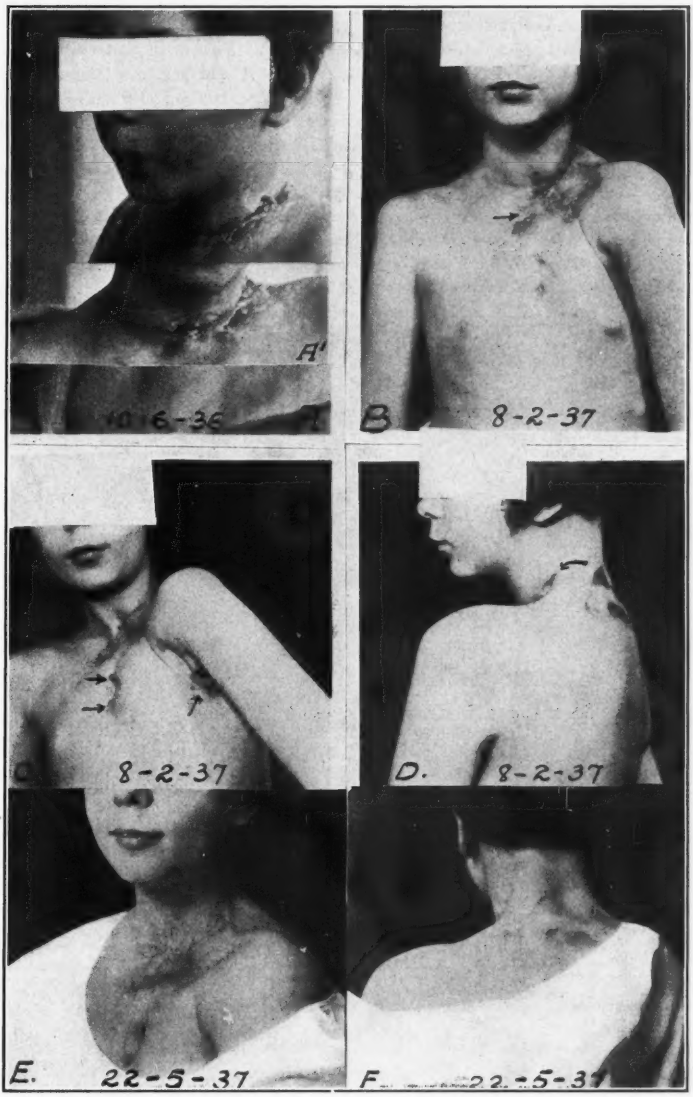

Fig. 6.—*A* and *A*[1] show the appearance of the patient's neck on June 10, 1936, one year after the onset of her illness. Previously, her head was drawn over acutely to the affected side. The skin lesions subsequently became more extensive. New areas appeared over the sternum, back of neck and in the axilla.

B, *C*, and *D* (Feb. 8, 1937.) were taken two weeks after treatment with prontylin had been started. Considerable healing has already taken place. Note how numerous and extensive the lesions had been. Evidences of the sinus formations are visible in the axilla, back of neck and over the sternum. These lesions were all originally similar to and more prominent than those noted in *A* and *A*[1]. The gain in weight and well being of this young patient are clearly visible in *E*, taken on May 22, 1937. The scars are not ugly, and from their present appearances (*E* and *F*) there is every indication that a plastic operation will not be necessary in this case.

The patient was again discharged from the hospital on August 29, 1936, quite ill. It was appreciated that new collections of pus were continuing to develop.

Reexamination of the chest and ribs on September 24 showed that the changes in the first and second ribs left were more extensive. Further, that there appeared to be some periosteal reaction about the third rib. Dr. Liebman also reported an area of increased density over the region of the first and second ribs and a line of thickened pleura, extending along the lateral margin of the lung, which suggested pocketing of fluid (Fig. 3). The left clavicle continued to show the periosteal reaction previously noted, and the left diaphragm remained quite high. Another film taken on October 24 suggested the possibility of a mediastinal effusion. Still another film taken on November 18 revealed the presence of a small cavity with a fluid level in the third interspace posteriorly. It was suggested that this shadow represented a collection in the soft tissues.

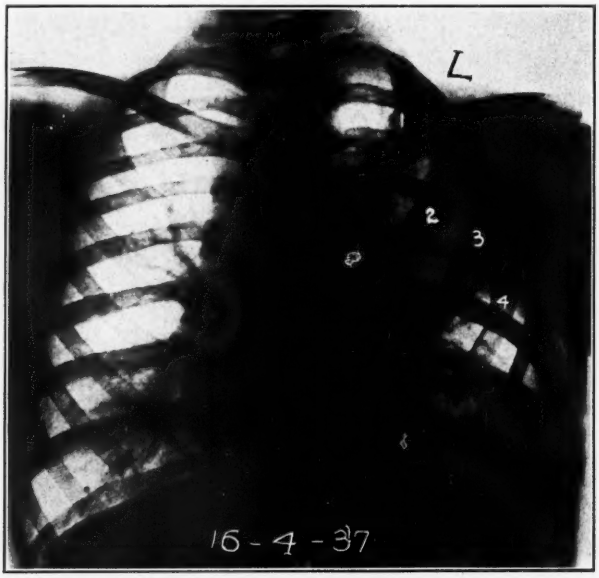

Fig. 7.—(April 16, 1937.) Treatment with prontylin was begun on Jan. 25, 1937. At that time the roentgen ray findings were even more marked than those noted in Fig. 4. Beginning clearing was noted within one week after treatment was started. At the present time the roughening and broadening of the first four ribs are present, but to a lesser degree. The density noted above is also less marked. Note that the periosteal reaction about the clavicle is not as prominent. The left diaphragm remains high, but does not exhibit paradox movement.

In November she returned to her home in Halifax, Nova Scotia. Her fever then ranged between normal and subnormal in the morning, and 104° in the evening. Her cough became more distressing, and she was brought back to Montreal (Fig. 4). It was suggested to the parents that the child be taken elsewhere for an opinion. She was taken to Dr. Churchill, of Boston. In the communication to Dr. Churchill, it was noted that during the previous three weeks she had lost another five pounds in weight. Also that a new lesion had made its appearance at the lower end of the sternum. There was no demonstrable evidence of osteomyelitis in this region, but it was suspected. The liver appeared larger than before, and also the kidneys. The urine showed a heavy trace of albumin. Amyloidosis was considered, but not demonstrated.

Dr. Churchill's interpretation of the problem was, for the most part, in accord with our own views on the subject, namely, that deep sepsis had originated in the supraclavicular and subpectoral lymph nodes. He regarded further surgical drainage as imperative, but advised further study of the patient's immunologic reaction to the infecting organism. Dr. Lyons, who saw the patient with Dr. Churchill, was of the opinion that, from an immunologic point of view, the lesion might be compared with the so-called chronic undermining ulcers and the persistent sinuses from lymph nodes harboring hemolytic streptococci. Immunotransfusions were recommended.

We again confirmed the fact that the patient's immunity to her infection was low. A fresh lesion had made its appearance over the midportion of the sternum, another at the back of the neck in the midline. Blood transfusions were given on October 28, November 7, November 25, and December 29, 1936. No great change was noted. The child would not permit us to irrigate the wound, nor would she go to the hospital for treatment. We did not force the issue, for her aunt, who was living in the same house, had suffered a nervous breakdown.

An outstanding success with the use of prontosil and prontylin in a child suffering from unresolved pneumonia, and a pleural effusion due to the hemolytic streptococcus, prompted us to try the effect of one of these measures in this case of chronic suppuration, now eighteen months from the onset and showing no signs whatever of improvement.

Accordingly treatment with prontylin was begun on January 25, 1937. During the first day she received 0.9 gm., then one tablet of 0.3 gm. every four hours, both by day and night, making a total of 1.8 gm. per day.

Within twenty-four hours the fever, which now had been running a septic course for many months, fell to normal and has remained so ever since (Fig. 5). Almost immediately her cough ceased and has not returned. Within two days the sinuses stopped discharging, except for a small one at the lower end. The ulcerated lesions changed with dramatic suddenness from indolence to marked activity. It was evident that they were healing rapidly (Fig. 6). Dressings required changing every second day instead of several times a day as previously. For the first time since the onset of her illness, feeding ceased to be a problem. Her appetite became ravenous. From a bedridden invalid she was transformed almost in a flash to a healthy active playing child. Her color became rosy. She gained 19 pounds in four and a half weeks.

Within a week it was noted that the density of the left chest began to clear. The clearing appeared to start on the mediastinal side at apex and base. The left diaphragm now moved more freely. It was at a slightly lower level. By the middle of February the problem became chiefly one of awaiting roentgenologic evidence of complete clearing, much as one would in the case of pleuritis. During the entire month of February "prontylin" treatment was continued, one tablet four times daily. Fluoroscopic examinations on February 3 and February 10 showed further clearing as did a roentgen ray film taken on February 26. Treatment with prontylin, 1.8 gm. per day, was continued until March 20. The dose was then reduced to 1.5 gm. daily, and treatment was stopped on April 5. A further gain in weight was noted, the wound was now healed everywhere, save for a small area over the lower end of the sternum. A roentgen film taken on April 16 showed that almost complete healing had taken place (Fig. 7). Although prontylin was given over a period of almost three months, this patient did not develop any toxic manifestations attributed to this drug.

It is unnecessary to comment upon this case. It is worthy of note, however, that in a recent publication on chronic undermining burrowing ulcers, Meleney and Johnson state that they have started to employ prontosil and its derivatives in conjunction with zinc peroxide in these

cases. They note further that, "although it is not as active against microaerophilic organisms as against ordinary streptococcus, there is evidence that it may be used in conjunction with zinc peroxide to prevent a spread or recurrence, particularly in those areas which cannot be adequately reached by zinc peroxide."

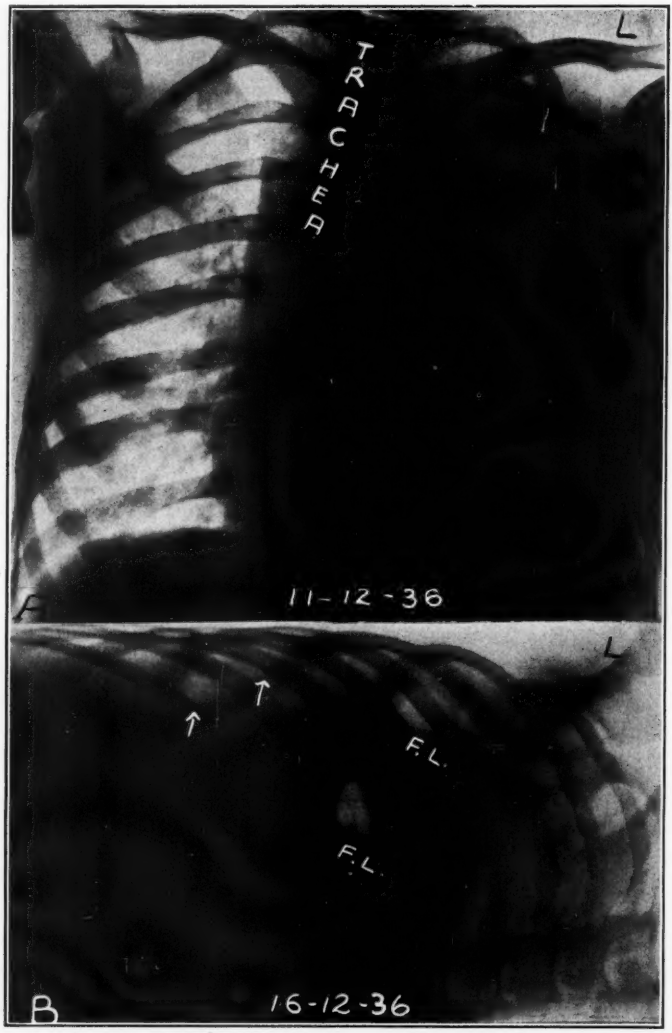

Fig. 8.—*A*, Note the displacement of the trachea and the heart to the right. The lesion in this case was unresolved pneumonia with pleural effusion, left; *B*, This film taken following repeated aspirations when only clear or blood-tinged fluid containing hemolytic streptococci was recovered, shows two fluid levels (F.L.) following air replacements. The two arrows indicate the sites of other aspirations and air injections. There are no fluid levels at these points.

CASE 2.—M. O., a female, aged ten years, was taken ill with left lower lobe pneumonia on November 25, 1936. For a week she ran the typical course of the disease. She then became more acutely ill, the pneumonic process spread. A pseudocrisis made its appearance sixteen days after the onset of her illness, and by this time the physical signs were those of a pleural effusion. She was, therefore, recommended for admission to the Homeopathic Hospital on December 11 (Fig. 8). On this same date 15 c.c. of blood-tinged clear fluid were obtained from the left pleural cavity. This fluid showed no growth. The cellular element was chiefly polymorphonuclear leucocytes. The temperature upon admission was 102°, the pulse rate 160, and respirations 50 per minute. A roentgen ray film of the chest revealed a unilateral opacity, with some displacement of the mediastinal contents to the opposite side. The leucocytes numbered 17,000, but the count soon rose to 23,000. The blood picture was that of a severe infection.

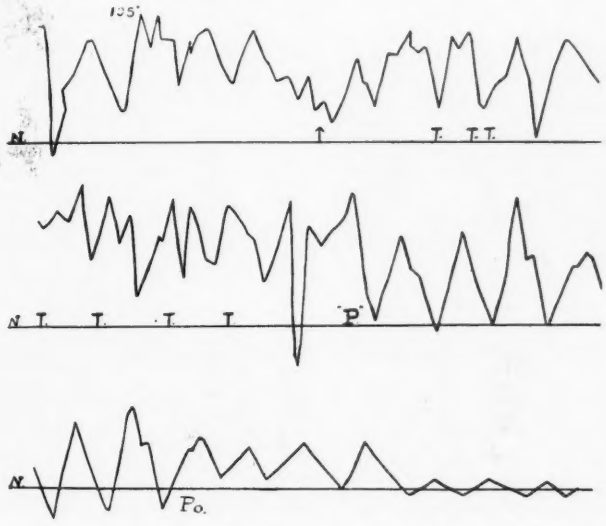

Fig. 9.—Note the septic temperature in this case and the pseudocrisis indicated by the arrow. Repeated thoracenteses, *T*, were all productive of clear or blood-tinged fluid. This fluid contained hemolytic streptococci. None of the aspirations affected the temperature curve. The start of treatment with prontosil is indicated by the letter *P*. Although the clinical improvement was prompt following the use of prontosil, the temperature remained elevated until shortly after prontylin, *P.O.*, was given.

Another thoracentesis was performed at a different site on December 13, on which occasion 15 c.c. of amber-colored fluid were obtained. On the following day only a few cubic centimeters of thin clear fluid could be obtained. None of the aspirations affected the temperature curve.

The intradermal tuberculin test at this time was negative. There was no expectoration. On December 15 and 18 repeated aspirations were productive of the same type of clear fluid, which on culture revealed hemolytic streptococci. As on previous occasions air was injected wherever fluid had been obtained. It was possible to recognize the site of each aspiration. There were but few fluid levels, and these denoted small localized pockets. For the most part the injected air appeared as small, round, clear shadows in a dense mass. The aspirations had been performed both front and back over the apex, base and on the mediastinal sides.

A pocket of pus could not be located. On December 21 the patient's condition became desperate. She was dyspneic, her pulse was rapid, irregular, weak, and thready. She was having chills and perspiring profusely. We expected to lose her at any moment. A further search in a desperate attempt to locate a pus pocket was made, but only 110 c.c. of clear fluid were obtained at one site, 30 c.c. of bloody fluid at another. The possibility of a foreign body had been excluded. The fluid obtained at this time was examined by Dr. Waugh, in a search for tumor cells. He reported serous fluid containing comparatively few cells of the nature of monocytes and hydropsical endothelial cells.

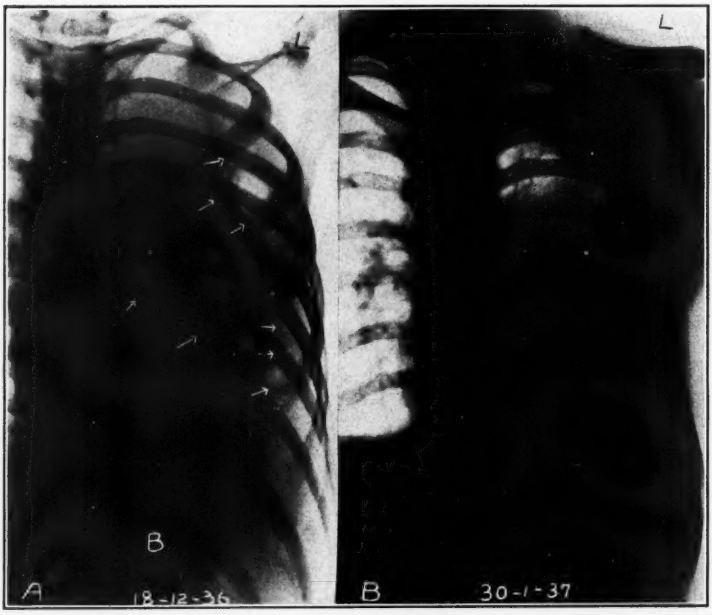

Fig. 10.—*A* (Dec. 18, 1936.), Note the numerous air pockets without fluid levels, indicated by arrows. These are the sites of repeated aspirations. On each occasion small quantities of clear fluid were obtained and air injected. The mediastinal contents are drawn over to the affected side. *B* (Jan. 30, 1937.), Treatment with prontosil was started on Dec. 24, 1936. The last thoracentesis was performed on Dec. 21, 1936. Note the clearing, and beginning aeration of the left lung.

Although repeated blood cultures were negative, the temperature curve, the extreme degree of toxemia, pallor sweats, and chilly sensations, all pointed to a septicemia complicating what we were forced to regard as an unresolved pneumonia. By this time we were satisfied that the repeated aspirations had excluded the possibility of an empyema.

As a last resort treatment with prontosil solution was undertaken on December 24, 1936, one month after the onset of her illness. During the first twenty-four hours she received six intramuscular injections, 5 c.c. each of a 2.5 per cent solution. Within twenty-four hours the child appeared less toxic. Her pulse became stronger. Within three days chills and sweats ceased. She developed an appetite. Her condition was remarkably improved and no longer occasioned any concern as regards life. From December 25 to 29, inclusive, prontosil was given in similar doses every six hours. There was no untoward reaction, the leucocyte count was now 12,000. She

continued to run a slightly elevated temperature, following her discharge from the hospital on January 10, 1937. She then was given prontylin, 0.3 gm. every four hours, four times daily. Within two days her temperature dropped to normal (Fig. 9). Prontylin therapy was kept up for four weeks after discharge from hospital, because the roentgen ray still showed delayed resolution of the pneumonic process. That the so-called unresolved pneumonia might terminate in a Corrigan's cirrhosis, with bronchiectasis or multiple lung abscesses, now became the chief problem. We are satisfied that the prompt improvement following the use of prontosil in this case was more than a mere coincidence. This improvement was clinically manifested by a lessening of toxemia. The gradual resolution of the underlying pneumonic process may have been due to an indirect rather than to a direct action (Fig. 10). It is obvious that more generous doses might have been employed at the start of the treatment (Fig. 11).

CASE 3.—M. B., male, aged six years, was admitted to the Jewish General Hospital on January 18, 1937. The chief complaints were fever, cough, pain in the

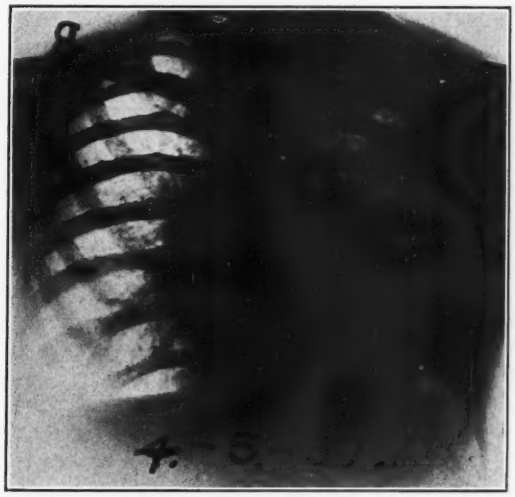

Fig. 11.—(May 4, 1937.) Note the further clearing which has taken place in the left chest. The heart still remains drawn over to the affected side. (The films in this case were taken by Dr. Adams.)

left chest, difficulty in breathing, and abdominal pain. The latter complaint had been present on and off for three weeks. There was no nausea or vomiting. Two weeks previous to his admission to the hospital, he had contracted a cold, and then showed signs of pneumonia at the left base with some meningismus. Pain and dyspnea were more marked on the day preceding his admission to the hospital. He appeared acutely ill and cyanosed; respirations were labored, accessory muscles of respiration were all at work. The upper respiratory tract appeared acutely inflamed. There were dullness and diminished breath sounds over the lower half of the left chest. A diagnosis of pneumonia with pleural effusion was made. The right lung was hyperresonant throughout. The mediastinal contents were not displaced. There was no rigidity of the neck, and no evidence of an intraabdominal lesion. The leucocyte count on admission was 30,900.

A roentgen ray examination of the chest the following day confirmed the presence of a small pleural effusion at the left base, secondary to a pneumonic process. The heart was slightly displaced to the right. Four days later there was evidence of a

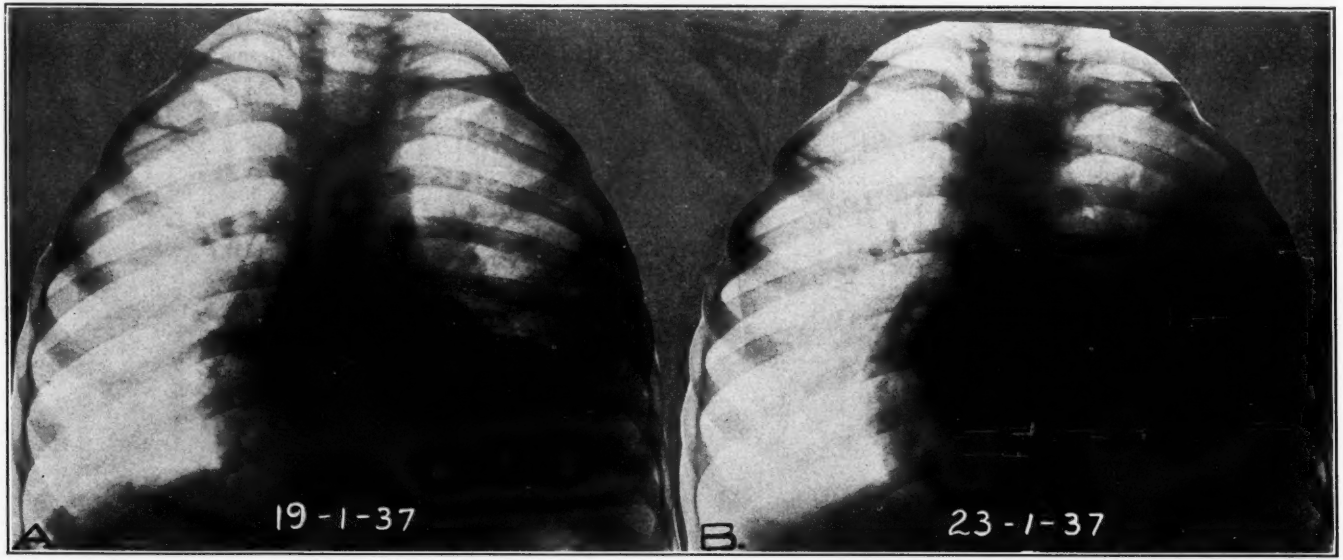

Fig. 12.—*A*, shows the involvement of the left lower lobe. The costophrenic angle is obliterated; *B*, taken four days later, shows a spread of the pneumonic process and the presence of an encysted pleural effusion. The presence of fluid was confirmed by a thoracentesis.

definite increase in the amount of fluid present in the left pleural cavity (Fig. 12). The leucocytic count persisted at the same level. The Mantoux test was negative, a blood culture showed no growth. A culture from the throat showed staphylococcus albus, nonhemolytic streptococci and streptobacilli. A thoracentesis was performed on January 20. Four cubic centimeters of blood-tinged fluid, slightly purulent, were recovered. The physical signs remained unchanged and for a day only the child appeared better, the temperature hovering between 98° and 102°. Prontylin, oral, one tablet three times daily, was started on January 25, and continuing until February 26, 1937. On that day he appeared better and on the following day, more acutely ill. He then received eight intramuscular injections of prontosil in 5 c.c. doses at six-hour intervals, followed by two similar doses intravenously. On January 27 and 28 the temperature rose to 105°. It dropped to normal on the succeeding day (Fig. 13).

Frequency of urination was noted during the time that the prontylin injections were given. The inguinal and right axillary lymph glands became enlarged. These glands drained the sites of the injections. A roentgen ray examination of the chest on January 29 showed a diminution in the amount of fluid present. A subsequent film taken on February 6 showed a slight reaccumulation of fluid. A thoracentesis two days later resulted in a dry tap. A film taken on February 17 revealed some thickening of the pleura and the presence of a few adhesions. Still another film

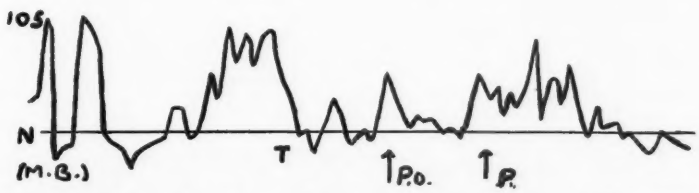

Fig. 13.—(M.B.) Note the two drops in the temperature curve before prontosil or prontylin was given. The drop following the thoracentesis, *T*, could not be attributed to the procedure, or to the nature or amount of fluid withdrawn. *P. O.* indicates when prontylin (oral) was given, and *P* when treatment with prontosil was started. Further details are noted in the clinical history.

taken eight days later and one taken on February 25 failed to show any evidence of fluid. There was some residual thickening of the pleura at the left base; the contour of the left diaphragm was slightly irregular. He was discharged on February 26, 1937 (Fig. 14).

We draw attention to the fact that there were two drops in the temperature curve before prontosil or prontylin were given. Mechanical dyspnea was never a problem in this case. Although a roentgen film on January 29 showed a definite diminution in the amount of fluid present in the pleural cavity, one taken on February 6 suggested a very slight reaccumulation. Treatment with prontosil and prontylin had been started on January 25. The course of the disease does not permit one to satisfactorily judge the effect upon the underlying pneumonic lesion. At the time treatment was started the general condition of the patient was not good, the degree of toxemia was marked, and signs were definite and extensive. There was some doubt as to the outcome. The disappearance of toxemia following therapy was prompt. Changes in the physical signs, however, were gradual.

We do not suggest that prontosil and prontylin prevented the development of an empyema. We were impressed with the fact, however, that even during January 27 and 28, when the temperature curve was as high as it had ever been, the child did not appear nearly as ill as he had been previously. Many more similar observations over a number of years are necessary before the true benefits of prontosil and prontylin therapy can be judged in this type of case. Gmelin reported his experience with two somewhat similar cases, occurring in children. Oral prontylin was used. At the start the fluid was thin. In one instance the temperature dropped to normal by lysis in three days, and in the other, six days after treatment was started. In one case the fluid became purulent, and it was necessary to establish drainage.

More recently Mellon reported that prontosil and prontylin are proving effective in the treatment of Type III pneumonia. "Of nine Type III pneumonia patients treated with the chemicals, seven recovered and two died. These figures are exactly the reverse of those for a group of nine patients who were not given the chemical treatment. In this group seven died and only two recovered."

In a group of fourteen rats infected with Type III pneumonia, the death rate was 85 per cent; in another group of thirteen rats with Type III pneumonia, prontosil brought the death rate down to 23 per cent.

CASE 4.—R. X., a female, aged twenty-seven years, was admitted to the Jewish General Hospital by ambulance on January 12, 1937, because of a right-sided pneumonia complicating pregnancy at the eighth month. She was under the care of Dr. Finkelstein. The complaints referable to the respiratory system, namely dyspnea, pain in the chest, and cyanosis were all of less than thirty-six hours' duration. The day previous the patient had had a chill and began to cough and expectorate blood-streaked sputum. She also complained of pain in both ears. Her temperature was 103°, pulse 120, and respirations 50. Physical examination revealed impaired resonance and blowing breathing at the right apex; elsewhere, over the right lung the breath sounds were harsh in character. On the day of admission the leucocyte count was 21,000, there was a moderate degree of anemia. The urine showed a two plus albumin. The sputum was found to contain a pneumococcus Type I. The patient received 60,000 units of serum in divided doses, over a period of fourteen hours. The following morning her temperature was normal, pulse rate was 100, and respirations had dropped to 40 per minute. On January 13, at 5 P.M., the patient went into labor and was delivered of a living female infant. The patient was then under the care of Dr. Ward. The infant died three days later of a bilateral confluent bronchopneumonia.

On January 14 the physical signs referable to the right chest were more extensive, the temperature remained only slightly elevated until January 19. The day previous her left ear started discharging. The presence of a pleural effusion was suspected and confirmed on January 23, when 1050 c.c. of moderately thick purulent fluid were obtained. An air replacement was performed at this time. Eight hundred cubic centimeters of thick pus were aspirated on January 25. The pus contained staphylococci and streptococci; this aspiration was followed by a drop in temperature. A rib resection and drainage of the empyema cavity were carried out under nitrous

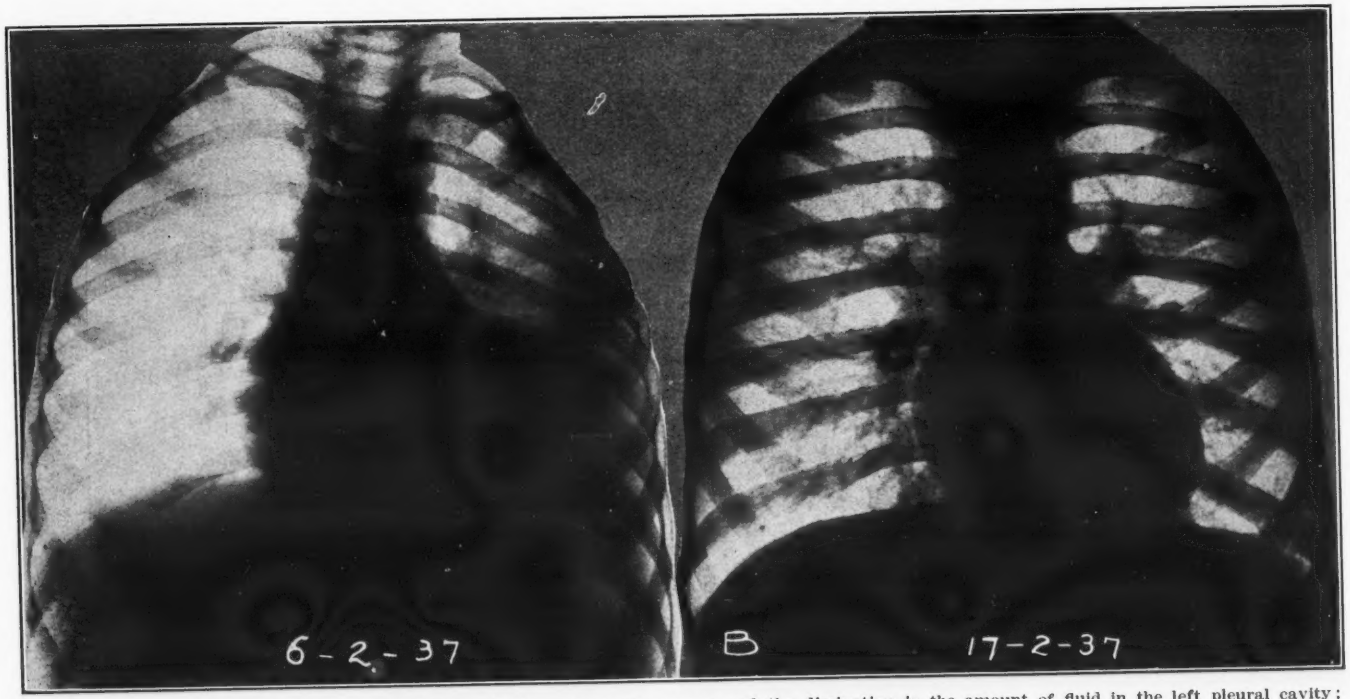

Fig. 14.—*A* (Feb. 6, 1937.), Note the resolution of the pneumonic process and the diminution in the amount of fluid in the left pleural cavity; *B* (Feb. 17, 1937.), Note the normal appearance of both lungs.

Fig. 15. Fig. 16.

Fig. 15.—Note the large pleural effusion, right. This followed a pneumonia which complicated a pregnancy.

Fig. 16.—This film was taken after the rib resection and drainage for empyema thoracis had been performed. It represents the appearance of the chest at the time the patient developed the septicemia.

oxide anesthesia on January 28, 1937. About 400 c.c. of pus were obtained. It was estimated that the cavity measured 800 to 1,000 c.c.

The clinical course was satisfactory until February 7, when the patient developed difficulty in urination, fever of 103°, and chilly sensations. Her pulse was of poor quality. She did not improve and so was given prontylin every four hours while awake, starting February 13. This was continued until February 21. The next day she complained of a sore throat. Treatment with prontylin was again started in doses similar to those noted above.

Although the empyema cavity was not completely obliterated and still measured 70 c.c., the patient was well enough to be permitted to be up and about on March 3. She was still receiving prontylin (Figs. 15 and 16).

On March 8 she complained of pain in the calf of the left leg. The following day she felt chilly, dizzy, and had pain in the right chest.

On March 10 she complained of a sore throat and had blood-streaked sputum. She had tonsillitis and the regionary lymph glands were found to be tender and palpably enlarged. Chills made their appearance on the following day, and bloody expectoration continued. On March 14 she appeared very acutely ill. She was still receiving

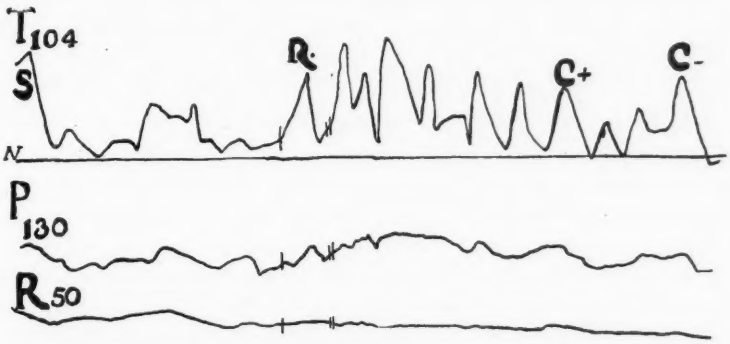

Fig. 17.—*S*, indicates the pulse, temperature, and respiration curves when the patient received serum for her pneumonia. Then followed a period when the temperature curve was depressed. When the elevations were noted, thoracenteses demonstrated the presence of pus in the pleural cavity. After the rib resection, *R*, was performed, there was a period of well being, soon to be complicated by the picture of sepsis referred to in detail in the text. Small doses of prontylin were given at the start. These were increased when the first positive blood culture, *C+*, was obtained. It is worthy of note that the patient's symptoms were promptly relieved by adequate doses of prontosil and prontylin. The blood culture soon became negative as indicated by *C-*, yet the temperature was still elevated. At this very period the patient was free from complaints.

prontylin, but the doses had as yet not been increased. The dosage employed at this time was obviously inadequate, and we confess that during part of this recent acute episode, we had not considered the possibility of a septicemia. The hemoptysis was apparently due to pulmonary infarction. It is not unlikely that the temperature might have reached higher peaks during the afternoon had the patient not been receiving prontylin. Starting on March 12 she had been receiving only three tablets daily.

A blood culture taken two days later was reported as positive for the streptococcus hemolyticus. She was immediately given prontosil solution, 10 c.c. intramuscularly every four hours, both by day and by night. She also received prontylin orally, six tablets daily, and 10 c.c. of the solution was instilled into the empyema cavity at each irrigation. A blood culture taken on March 18 was reported as negative. It is worthy of note that, although the patient felt and looked much better, her tem-

perature was still elevated. It is possible that had the patient not been receiving prontylin, the blood culture might have been more strongly positive. We cannot prove this point any more than we can deny that it might have become negative without treatment. The temperature dropped to normal on March 19, and has remained so ever since (Fig. 17). Prontosil therapy was discontinued on March 27. Appreciating that prontosil is a dye which stains and that it might be possible to stain the organisms in the blood so that they could not be recognized, the blood culture was again repeated several days after all treatment had been stopped. It again proved negative. When the patient was discharged from the hospital on April 2 a small empyema cavity still remained.

Expansion of the lung was slow in this case. The discharge from the empyema was always scanty when prontosil or prontylin was given. In this connection, we may note that we observed a striking sudden diminution in the amount of discharge in one case of breast abscess, following the administration of prontylin. On the other hand, we have observed almost complete cessation of a previously profuse discharge in the case of severe otitis media, following the administration of prontylin, but the condition progressed, the discharge returned, and it became necessary to perform a mastoid operation. To date we have been pleased with the results obtained in the treatment of erysipelas.

SUMMARY

Some experiences with prontosil and prontylin in the treatment of infection of the lung, pleura, and chest wall caused by the hemolytic streptococcus are recorded. These concern both acute and chronic infections. Case 1 presented several features worthy of further emphasis. The skin and bone lesions constituted an unusual complication of scarlet fever. Pus collected in surgically inaccessible regions. Simple operative procedures on two occasions confirmed this point as well as the clinical impression of poor resistance on the part of the patient. The condition was chronic but uncomplicated by microorganisms other than the hemolytic streptococcus which was obtained in pure culture. Numerous recognized therapeutic measures had not only failed to halt the progress of the disease but had also failed to build up the patient's resistance. A dramatic response to prontylin was obtained in this case. The dosage employed sufficed, yet it may be regarded as somewhat inadequate under most circumstances. In this case prontylin was employed daily for almost three months. No ill effects resulted. Further unrecorded personal experiences are more than suggestive of the value of prontosil and prontylin in the treatment of chronic infections due to the hemolytic streptococcus. In Case 2, one of so-called unresolved pneumonia complicated by a pleural effusion, prontosil and prontylin were employed as a last resort. Surgical interference was not indicated. This type of case would under ordinary circumstances have been treated by supportive measures, with the hope that the patient's resistance would eventually become greater than the virulence of the infection or that localization would take place with the development of an empyema. The

need for some such agent as prontosil or prontylin in this type of case is obvious. Case 3 allows considerable discussion. It indicates the need for numerous control cases. It can hardly be argued, however, that a measure which may prove helpful should be withheld until more control cases are available. The apparently beneficial response noted in Case 3 may have been a mere coincidence. Case 4 demonstrates the need for careful clinical observation of patients receiving prontylin. The temperature response to prontosil and prontylin is not always uniform. This may be due in part to variation in dosage Small doses sufficed in Case 1. We are of the opinion that prontosil and prontylin contributed to the clearing up of the septicemia in Case 4. Whenever these drugs are employed, it should be appreciated that they may render a typical temperature curve atypical. Further, that when a positive blood culture has been rendered negative, repeated cultures should be obtained after all therapy has been stopped for several days. This is particularly true in the case of prontosil which stains. The patient referred to in Case 2 will have to be watched for the possible development of pulmonary fibrosis and bronchiectasis. In Case 4 prontosil was instilled into the empyema cavity. We are of the opinion that treatment with prontosil and prontylin should be kept up as long as significant signs and symptoms persist. The temperature curve does not serve as the only guide in this connection, particularly in the presence of an exudate.

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DISCUSSION

DR. HARRY R. DECKER, Pittsburgh, Pa.—I want to ask Dr. Ballon whether any blood studies had been made after the use of prontosil and prontylin in these cases, the reason being that in some of our work in general surgery, we have had develop, we believe, an aplastic anemia, which may in the future be detrimental to the patient. I do not mean to imply that these cases are not in need of something very specific and urgent in their treatment, and that these drugs should not be used. But it would be interesting to know whether the experience of Dr. Ballon and Dr. Coryllos shows any unfortunate blood transformation taking place.

DR. J. W. NIXON, San Antonio, Tex.—This case has the appearance of a burrowing ulcer. Nineteen of these cases of burrowing ulcers have been reported by Meleney and Johnson, and in each instance the causative organism was an anaerobic streptococcus.

DR. JACOBAEUS, Stockholm.—I must confess that I am not so experienced with sulfanilamide (prontosil) in streptococcic infections. We have tried it in some cases of streptococcus viridans in endocarditis, but we have not yet had any result. In the cases of infection in the chest wall and in the pleura, we employ mainly, as I said before, the surgical treatment; therefore, I cannot give you any experience in such cases.

DR. JOHN V. BOHRER, New York, N. Y.—I should like to ask Dr. Ballon if he has any explanation for the apparent variation in this drug. To illustrate what I mean, we had a child ten weeks old who first came to the hospital with an erysipelas. This child responded exceedingly well, miraculously in fact, to prontosil, and was discharged. Soon, thereafter, she was readmitted with a hemolizing streptococcic pneumonia. We felt that prontosil would again control the infection. At first, it reduced the temperature and it looked as though we were going to have another spectacular result. The pneumonia, however, ran a normal course; the child developed an empyema. Again we tried the prontosil and prontylin, but they seemed to have no effect whatsoever. The dosage was large and she developed a rather

severe drug rash, which subsided promptly when the drug was discontinued, but it certainly had no curative value.

The other point is about the toxicity. Anemia has been mentioned. I gave this drug in rather large doses, as recommended, to a patient who had a hemolizing streptococcic septicemia. The patient went into a moderately deep coma and was exceedingly sick as a result of the infection. We all felt that the coma was due to the streptococcus intoxication, but the confusing thing was that his pulse remained very good. We stopped the prontosil, and in two days he became conscious. He not only had been in a coma, but he also had had a contraction of the masseter muscle and could not open his mouth. Both of these symptoms were directly due to the prontosil, because we repeated the drug after he recovered and the same symptoms recurred.

After spectacular results with several cases of erysipelas, the above mentioned results were discouraging. The drug has been entirely negative in a group of five cases of hemolizing streptococcic empyema.

DR. L. J. LEAHY, Buffalo, N. Y.—We have had occasion to study six cases of empyema which were treated with prontosil and prontylin. When a case was first proposed to me, I couldn't conceive of "curing empyema with pills," so I was a bit stubborn the first time, and performed an open drainage. The pus was thick enough to warrant that type of treatment, but I finally condescended to remove the tube about the third day, and let them treat it. The lung promptly reexpanded, the sinus closed, and the child went about perfectly well.

Following that, we had three more patients with positive aspirations for hemolytic streptococcus, and the only treatment that was instituted was the administration of prontosil and prontylin and diagnostic aspirations. There were no irrigations, no evacuation of the empyema cavity, and the three children promptly absorbed their fluid, their lungs expanded, and they went about perfectly well.

The fifth patient was a child who is now under treatment. I cannot tell as to the end-results, although there was a very high growth of hemolytic streptococcus on the blood culture, and it is rapidly diminishing both the number of colonies and the rapidity of their growth. This child, who from all appearances was doomed to death, is now apparently making a recovery.

The last case we have is now under treatment. It is a hemolytic streptococcic empyema in an adult who has an active tuberculous infection in the other lung. I haven't been able to demonstrate tuberculosis of the pleura on the empyema side. Although the patient has only been under treatment for about five days, on the second day the temperature, which had been around 103° and 104°, came down to normal. I am very anxious to see what the results will be in that case.

DR. RICHARD H. MEADE, JR., Philadelphia, Pa.—May I ask Dr. Ballon what he considers adequate dosage in these cases to which he refers—the adequacy of the treatment?

DR. DAVID T. SMITH, Durham, N. C.—As a bacteriologist and a medical man, I have naturally been interested in this problem. The personal reports all over the country correspond exactly to those brought up by the discussers, namely, that this is a highly effective as well as a relatively dangerous drug. The important thing would seem to be the level of the active principle of prontylin in the blood. Dr. Marshall has worked out a method by which relatively quickly one can assay the level of the active principle in the blood. Therefore, it would seem desirable to give the minimum amount of the drug which will maintain the optimal killing power of the drug in the blood. That level will vary with different patients.

A group of students at Duke, normal, healthy medical students, have been taking this drug themselves and studying their reactions, and they have had some quite alarming reactions from a relatively small dose.

I think you may conclude in the end that this drug is probably like arsphenamine or salvarsan, highly effective and also relatively dangerous and will have to be evaluated slowly, just as we have done in the case of salvarsan.

DR. POL N. CORYLLOS, New York, N. Y.—I want to congratulate Dr. Ballon on his presentation.

As I said in presenting my study of 150 cases of tuberculous empyemata, I had the opportunity to try chemotherapy with prontosil and prontylin in five cases of mixed infection tuberculous empyema in which hemolytic streptococcus was present. The bacteriologic work and clinical follow-up of these cases was done by Dr. Fritz Meyer, of Berlin, Germany. The immediate results have been very satisfactory. Streptococcus had rapidly disappeared from the fluid in four of these cases, and a striking clinical improvement had followed.

The importance of this treatment in mixed infection tuberculous empyemata is obvious. It would allow a rapid disintoxication of these patients by shortening the toxic phase of this dreadful complication of pneumothorax treatment. Thus thoracoplastic obliteration of the empyema cavity should be carried on much earlier, before the patient is exhausted by prolonged septicity and by amyloidosis. Whether this treatment would be sufficient to avoid thoracoplastic treatment I am not ready to tell. Only the following up of these cases can solve this problem. In my experience the best results were obtained by the combined treatment of antistreptococcic serum prontosil and prontylin. I want to terminate this discussion by quoting a statement on the respective action of these therapeutic agents:

"1. The action of the streptococcus serum is antitoxic and increases the phagocytosis of streptococci.

"2. The action of prontosil (injections) and prontylin (tabloids) inhibits the toxin production and stops the growth of hemolytic streptococci.

"3. The combined treatment with streptococcus serum *and* prontosil or prontylin is by far more effectful than the treatment with either of the two alone.

"4. By this combined treatment the empyema fluid is sterilized in the course of 4 to 5 weeks.

"5. In vitro the sterilized empyema fluid of patients treated with the combination of streptococcus serum and prontosil inhibits the toxin production and the growth of hemolytic streptococci."

DR. HARRY C. BALLON, and DR. ALTON GOLDBLOOM, Montreal (closing).—I am glad our presentation provoked so much healthy discussion. I am particularly grateful to Dr. Coryllos. His experiences coincide with our own. We have a great deal to learn about the action of prontylin, and for that matter, about the response of tissues to infections caused by the streptococcus.

In reply to Dr. Decker's question, I should like to point out that the child referred to in the first case received prontylin for over three months. We were frankly afraid to discontinue its use chiefly because complete roentgenologic clearing of the lesion had not yet taken place. Dr. Colebrook, who, as you all know, has had considerable experience with these agents in the treatment of puerperal sepsis, recently addressed the Montreal Medico-Chirurgical Society. I discussed our first case with him. It was at his suggestion that we stopped treatment for a time. I believe I am correct when I state that his chief reason for suggesting that we stop therapy was the possibility of sulphhemoglobinemia. We subsequently gave this same child prontylin because of the return of slight discharge from one of the sinuses. There were no ill effects. Her blood picture has remained within normal limits up to the present time.

We have not observed any agranulocytic-like blood picture following the use of these drugs. Work remains to be done along these lines, however, since toxic effects have been observed by others.

Our experiences have been similar to those of Dr. Bohrer, namely, that there are occasions when one obtains a dramatic response to prontylin, yet another infection elsewhere in the body caused by the same microorganism or the same infection may be followed by a complication which will not respond to treatment. For example, a child develops a streptococcic sore throat and suppurative otitis media due to the same microorganism. The discharge ceases, and the temperature falls to normal following the use of prontylin. In a very few days there is evidence of mastoiditis which requires surgical interference.

Constant observation is necessary and one must individualize; each case is a law unto itself.

Although we have not treated any patients suffering from bacterial endocarditis, the experiences of our colleagues and those referred to in the literature are as disappointing as Professor Jacobaeus has intimated. Perhaps the presence of thrombi or emboli may have something to do with it.

Dr. Leahy's experiences too agree with our own. He has gone a step further, for we have up to the present favored drainage of streptococcus empyemas, and by empyema I mean laudable pus, pus in the sense that we have heard it so often referred to by Dr. Graham. I do not feel that we have yet reached the stage where we can say that a diagnostic aspiration, followed by the administration of prontylin, is the treatment of choice for true empyema thoracis. Prontylin can with profit be employed when the effusion is turbid, or contains small or microscopic quantities of pus.

The streptococci have been both aerobic and anaerobic. I have not observed any particular difference, and I believe that has been Dr. Coryllos' experience. The careful bacteriologic studies in the first case were carried out under the direction of Professor Murray, of McGill University.

It would be unfortunate if we were left with the impression given by Dr. Smith, namely, that we are dealing with a very dangerous substance. Dr. Bohrer's experience emphasizes the need for caution. The reaction which he referred to may well have been due to the drug. I am familiar with the occurrence of acidosis in individuals who show no symptoms. Untoward reactions will undoubtedly be reported, particularly when the drug is used indiscriminately. We have given it to a few normal subjects. There were mild reactions. We have not yet employed prontylin in the treatment of cancer, but some enthusiast who regards it as a cure-all will.

One must watch for cyanosis, particularly if the subject is a candidate for an operation under general anesthesia. Such a situation recently caused me considerable concern. Whether prontylin has a bacteriostatic or bactericidal action is to my knowledge at present not definitely known. Certainly prontylin has proved effective in the presence of a variety of organisms.

It is more or less agreed that the active principle is apparently sulfanilamide. Anyone using the drug should become thoroughly familiar with the work of Colebrook, Long, Bliss, and others. In reply to Dr. Meade's question upon adequate dosage, large doses are indicated, yet occasionally small doses accomplish the same thing. By large doses we mean 60 gr. or more in twenty-four hours. We refer to infections caused by the hemolytic streptococcus.

We have employed prontylin in a rather large series of cases. These include acute and chronic infections involving extremities, erysipelas, meningococcus meningitis, etc. Our results to date have been gratifying.

A NEW SIMPLIFIED TECHNIQUE FOR THE DRAINAGE OF LUNG ABSCESS EMPLOYING GRADUATED TROCHARS*

OWEN H. WANGENSTEEN, M.D.
MINNEAPOLIS, MINN.

SHOULD external drainage be done for pulmonary abscess and *when* should it be done are questions which have received considerable attention in current medical and surgical literature. *How* surgical drainage of a pulmonary abscess should be accomplished, one might reasonably conclude from the paucity of comment upon the subject, has rarely been deemed important enough to discuss. Nevertheless, every surgeon with experience in the treatment of pulmonary suppuration knows that the manner of opening a pulmonary abscess is no trifling matter.

USUAL SURGICAL CONSIDERATIONS

The following considerations are generally agreed upon: (1) Local infiltration with a solution of novocaine is the anesthetic of choice. When the administration of inhalation anesthesia is contemplated, the patient should be encouraged to evacuate the cavity, so far as is possible before the operation. (2) The approach to an abscess is to be determined after study of postero-anterior and lateral films of the chest. In the main, the following considerations ordinarily decide the location of the the incision: (a) Access to a pulmonary abscess in the upper lobe of either lung is most directly made through an axillary incision—occasionally through an anterior incision; (b) an abscess of the middle lobe of the right lung is most readily approached through an anterior or anterolateral incision; (c) pulmonary abscess in the lower lobe of either lung is best approached through a posterior incision. (3) A two-stage operative attack upon the abscess is mandatory except in a peripheral abscess which exhibits at operation definite obliteration of the pleural space beneath the area of rib resection. (4) The abscess itself may be reached at the second operation in one of two manners in accord with current practices and descriptions of the procedure: (a) the content of the abscess cavity is partially aspirated with a long needle; a grooved director is pushed into the abscess cavity beside the aspirating needle; this track is then enlarged with knife, scissors, cautery or the finger to permit evacuation of the abscess and external drainage; (b) the surface of the lung over the abscess is charred with the actual cautery or the surgical diathermy knife, and a tunnel is established by continuing this burning process until the abscess cavity is reached.

*From the Department of Surgery, University of Minnesota.
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THE AUTHOR'S METHOD

Dissatisfactions with the first of the two methods of draining a lung abscess described above have been, now and then, expressed by surgeons. In a judicious consideration of the clinical aspects of lung abscess, Brunn has recently called attention to the hazards of plunging a knife along a needle track to evacuate the contents of a lung abscess. About ten years

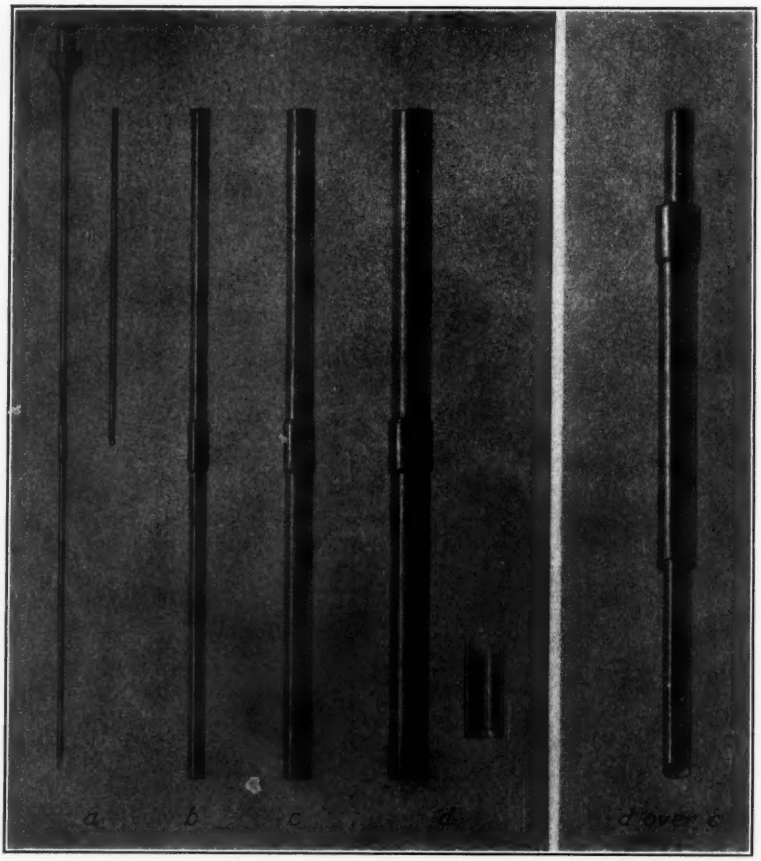

Fig. 1.—Graduated lung abscess trochars and aspirating needle with extra hubless shaft.

ago, while visiting a few surgical clinics on our Atlantic seaboard, the author had the unhappy experience of witnessing the sanguinary conflict which employment of this method of draining a pulmonary abscess caused an accomplished thoracic surgeon. The difficulty of dealing speedily with brisk bleeding into a cavity communicating with a bronchus in an anesthetized patient through a long narrow channel

proved too formidable a handicap. A year later, while spending a year abroad, the author was privileged to see the meticulous care observed by Professor Sauerbruch in establishing external drainage of a pulmonary abscess. Employing a Paquelin type of cautery, he slowly and deliberately burned an opening directly into the abscess cavity. These two contrasting scenes left an indelible impression upon the memory of the observer. Later, the author had an opportunity in his own clinic to ascertain that the method used by Professor Sauerbruch was an eminently satisfactory manner of draining a pulmonary abscess.

In 1931 an extremely ill patient with a large localized peripheral pulmonary abscess came under the author's observation. Drainage of the abscess seemed obligatory, but the patient's condition did not appear to justify the usual formal type of operation. Circumstances suggested the following procedure: intercostal aspiration of the lung abscess with a long needle; coagulation of the needle tract (the needle remaining in situ) with the surgical diathermy current. The skin adjacent to the needle was slit with a knife; the hub was broken off the needle and an empyema trochar was pushed over it through the coagulated tissue into the abscess; in turn, the diathermy current was applied to the trochar, the needle withdrawn and a small tube left in the abscess cavity, whereupon the empyema trochar was withdrawn. This expedient did not save the patient, but it suggested the plan of procedure which the author has since employed in establishing drainage of pulmonary abscess.

TECHNIQUE

The hazard of draining a pulmonary abscess in the manner in which a soft tissue abscess is evacuated has been described. The difficulty with the cautery or surgical diathermy method is that more lung tissue is destroyed than is necessary. It occurred to the author that a series of graduated trochars with a knifelike edge would serve the purpose simply and satisfactorily, aided with the coagulation current of the surgical diathermy apparatus (Fig. 1). The track of the aspirating needle into the abscess cavity could be followed by passing increasingly larger trochars over one another, applying the coagulating current in turn to each, until a sufficiently large tunnel had been established to permit of adequate drainage. Use of this method has demonstrated that bloodless drainage of pulmonary abscess may be quickly made in this manner with minimal destruction of lung tissue.

First Operation.—A study of postero-anterior and lateral films constitutes the best guide to the surgical approach. Employing procaine infiltration anesthesia, segments of 5 to 8 cm. in length are removed from two adjacent ribs overlying the abscess; the intercostal muscle bundle between the ribs is excised and the visceral pleura covering the lung can be seen to move with respiration if no adhesions are present (Fig. 2*a*). In the

experience of the author, it is almost invariably necessary to employ a gauze pack to assure firm agglutination between the visceral and parietal pleura to permit of safe external drainage of a pulmonary abscess. The presence of thin, fibrinous adhesions at the time of rib resection should not be interpreted as sufficient justification to do a one-stage operation. The writer has not felt that the suture method of securing adherence between the two serous coverings of the lung was safe or reliable enough to warrant its employment. A wisp of the gauze pack left upon the external surface of the parietal pleura should be allowed to project through the muscle plane overlying the site of rib resection. If the gauze pack is entirely buried by sutures beneath the reunited muscles, fluid may accumulate and delay the agglutination of the pleural surfaces. Saturation of the pack with irritating solutions, such as tincture of iodine, is to be avoided because of the serous exudation which ordinarily follows. A plain gauze pack left in intimate contact with the parietal pleura will usually assure adhesion formation within this short period of time. The skin is closed with interrupted sutures.

Second Operation.—Five to seven days later, the wound is reopened and the gauze is removed. The visceral pleura can no longer be seen owing to tissue proliferation in response to the presence of the pack. Mindful of the direction and depth at which the abscess cavity is to be reached, as indicated by interpretation of the roentgen films, an aspirating needle is carefully guided into the lung (Fig. 2*b*). Absence of resistance to the advancement of the needle indicates that the abscess cavity has been reached, as may also coughing by the patient. In large cavities air or pus may be readily aspirated. In the smaller multilocular abscess very little exudate is, as a rule, obtained at this juncture. The coagulating current of the surgical diathermy apparatus is now applied to the needle in sufficient strength to sear the tissue immediately adjacent to the needle. The upper half of the needle is unscrewed, and the extra attachment without the hub is substituted (Fig. 2*c*). The depth at which the abscess cavity was entered is carefully noted. The lower half of the smallest cutting trochar is now placed over the aspirating needle and is pushed into the pulmonary substance to the same depth. The proximal end of the trochar has a sharp edge, and its introduction through the bloodless field along the needle track is readily accomplished. The aspirating needle is now withdrawn and the upper half of the trochar is attached. The coagulating current is again applied and the lower half of the trochar next in size is passed over the smaller trochar. This procedure is repeated until the largest trochar has been introduced into the abscess cavity.* It is not

*These trochars were first made for the author by Mr. Rudolph B. Thorness in the Central Scientific Apparatus Shop of the University of Minnesota. The author's associate, Dr. J. R. Paine, suggested the extra shaft for the aspirating needle. In the case referred to earlier in the text in which the empyema trochar was used, the needle hub was forcibly broken off. It is a pleasure to acknowledge here the helpful cooperation and suggestions of Mr. Thorness and Dr. Paine. The George P. Pilling & Son Company have undertaken manufacture of these trochars, and information concerning them is to be found elsewhere in this Journal.

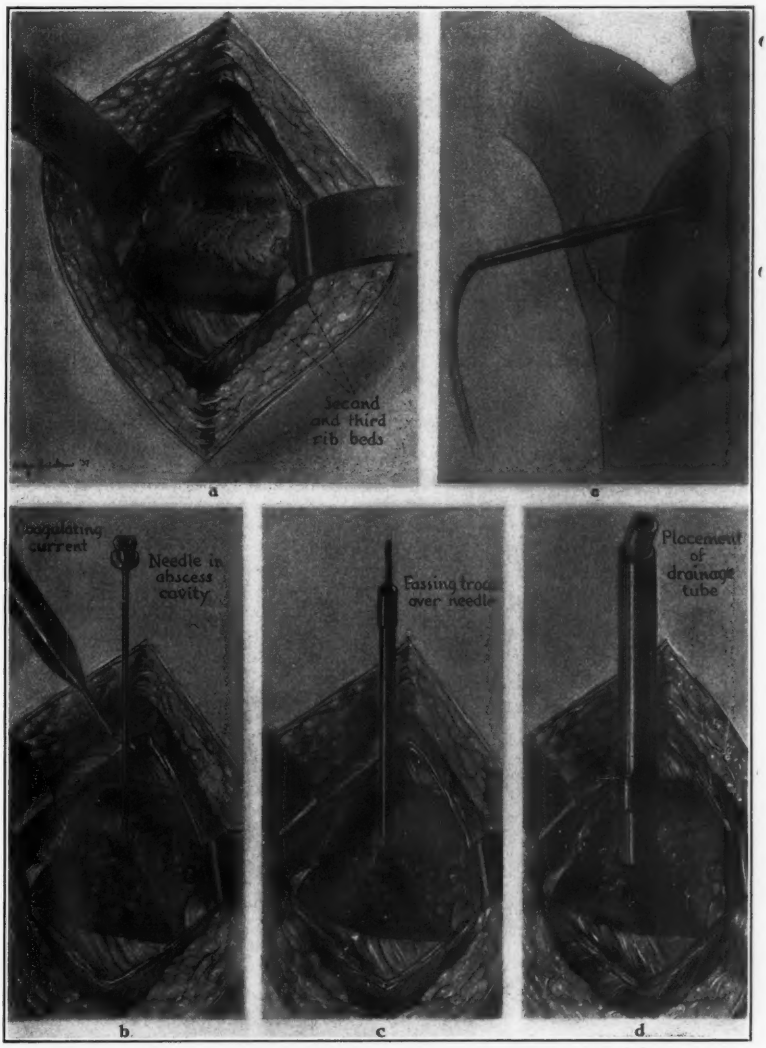

Fig. 2.—The technique of external drainage of a localized lung abscess. These drawings were made for the author by Miss Evelyn Erickson of the Department of Medical Art from an operation upon a right upper lobe abscess.

a, First operation; resection of second and third ribs and excision of intercostal muscle bundle through a short vertical incision in the axilla. A gauze pack is partially buried below the resutured muscles (see text).

b, Second operation; the aspirating needle has been directed into the abscess cavity and the coagulating current is being applied.

c, The upper half of the aspirating needle has been detached and the extra shaft has been screwed on. The smallest trochar is pushed over the needle through coagulated lung substance into the cavity.

d, The largest trochar in place; the drainage tube is being inserted.

e, When the abscess cavity is correctly entered, dependent drainage is obtained. Pulmonary abscesses which have not presented a single large cavity have also responded well to drainage by this means.

uncommon, as the large trochar enters the abscess, to have a large amount of disintegrating tissue in the process of being sloughed off, coughed out through the lumen of the trochar. The pulmonary tissue along the track of the largest trochar is finally coagulated (Fig. 2*d*). A drainage tube may be inserted through the trochar, or it is often found that a somewhat larger tube may be introduced when inserted directly through the tunnel into the pulmonary abscess.

A pulmonary abscess may be drained quickly in this manner, and without the hazard of intrabronchial bleeding; nor has there been secondary hemorrhage. Furthermore, a minimum of pulmonary tissue is destroyed in the surgery of access. One might be led to believe that only an abscess with a single large cavity can be well drained by this means (Fig. 2*e*). Trial has demonstrated, however, that multilocular abscesses may be effectually dealt with by dependent external drainage accomplished in the manner here described. For the large chronic pulmonary abscess with multiple areas of lung destruction, the Graham Cautery remains the most promising method of attack.

CHOICE OF DRAINAGE MATERIAL AND MECHANICS OF EVACUATION OF AN ABSCESS

Rarely has the author found it necessary to employ a gauze wick or pack for the control of bleeding in draining a lung abscess by the method here described. Alexander has recently expressed dissatisfaction over the employment of a rubber tube for drainage of a pulmonary abscess, feeling that the liability to hemorrhage was thereby enhanced. He recommends "snug packing of the cavity with moist gauze so as to occlude the mouths of the bronchi," believing that this procedure tends to establish an efficient mechanism for expectoration in that the act of coughing, in the presence of a pack, will drive the bronchial secretions toward the patient's mouth. When a lung abscess is drained by a tube, Alexander states that "the pulmonary secretions are not efficiently expelled through either the tube or the mouth, some of them may remain in the lung and be driven to hitherto unexpected portions of the lung, infecting them." Every expression from Alexander should be lent the greatest credence. This opinion relating to the efficiency of gauze in the drainage of a lung or other abscess is not one, however, in which the present author can concur. Incision of an abscess with provision for dependent drainage will invariably lead to effectual evacuation of the free exudate. Sloughs or exudate adherent to the walls of an abscess cavity will only gradually come away, as the reparative process is accelerated by adequate removal of accumulated pus and detritus. When mechanically satisfactory drainage has been instituted for the evacuation of the *free* exudate in a lung abscess, the rôle of the patient becomes an entirely *passive* one. The force of gravity aided by the medium of an open channel is the *active* agent. In the

separation of *adherent* exudate and dead or dying tissue, the immunologic defense mechanism of the body is the *active* force.

The continuance of considerable purulent exudate after adequate drainage has been established in a suppurative process usually indicates one of the following: pocketing of exudate interfering with drainage or the persistence of dead tissue. In a carbuncle of the skin which has been adequately incised, the excision of the dead tissue diminishes the drainage markedly. In a deep suppurative process, such as a lung abscess, the patient and surgeon are both usually quite willing to be somewhat more tolerant over the continuance of suppuration, after the establishment of adequate drainage, realizing that more formidable measures are necessary to deal with the situation than in suppuration in a tissue which lies nearer the body surface. Persistence of fever, sputum or cough as well as continuance of purulent drainage and failure of resolution of the suppurative process as indicated by subsequent roentgen films, after the elapse of some time following drainage, constitute indication for more energetic surgical intervention.

WHEN SHOULD A PULMONARY ABSCESS BE DRAINED?

For somewhat more than a decade, the principles which Macewen enunciated in 1893 for the surgical treatment of brain abscess have become more generally appreciated in the treatment of other visceral abscesses. Medical men today, generally, appreciate the futility of attempting to control acute pulmonary suppuration by surgical means. Only when localization has occurred, can active surgical intervention be contemplated without aggravating the effects of the infection. There is no uniform agreement concerning the length of time necessary for such localization to occur. In the main, it may be said that lack of extension as determined by roentgen evidence, together with an abatement of symptoms accompanying a spreading or threatening infection are the most reliable signs of localization. There can be no doubt that both medical men and surgeons have latterly been too withholding in urging surgical drainage. Rib resection and compression with gauze have been advised as a method superior to external drainage.

It is now fully appreciated on every hand that a large number of pulmonary abscesses will clear spontaneously on conservative treatment and employment of postural drainage. Undoubtedly, however, this "wait and see" policy is responsible for many of the large chronic abscesses which necessitate use of the Graham Cautery to bring about a favorable issue. When an intraperitoneal abscess forms following rupture of the vermiform appendix, with continuance of fever, external drainage is instituted when evidence of localization of the inflammatory process is definite, unless signs of resorption of the abscess

are evident. Such proof usually consists of the following: obvious improvement as indicated by subsidence of the toxemia which threatens life, as manifested by lowering and steadying of the body temperature; decrease of the pulse rate; improvement in appetite and a renewal of interest in the daily occurrences of life. These are, too, the signs which indicate that the natural defenses of the body are waging a winning conflict with a pulmonary abscess. In addition, the roentgen film and the character of the sputum afford important clues concerning delimitation of the inflammatory process. When evidence is clear that the inflammatory process is in check, why wait? Why not establish external dependent drainage? To be certain, a few abscesses may be operated upon, which, with more time may have cleared spontaneously; but, more important, a larger number will probably be saved the devastating effects of chronicity, in which the reparative process has only succeeded in isolating honeycombed abscesses with stiffened walls, which cannot be drained without the employment of radical measures.

Postural drainage, even when it effectually evacuates the contents of an abscess, is only intermittent. The more efficient drainage of a short dependent external fistulous tract, which constantly keeps the abscess drained, is but badly imitated by postural drainage (Fig. 3). The instances in which bronchoscopic aspirations pyramid the benefits of postural drainage are few. The value of bronchoscopy in treatment of lung abscess concerns essentially those cases which have their origin in an aspirated foreign body.

The author would not lend the impression that the surgeon plays an important rôle in the treatment of infection save in these two respects: (1) in promoting the evacuation of exudate from an abscess by drainage; (2) in preventing the spread of an infection, as when he removes the acutely inflamed vermiform appendix before it perforates. In the treatment of infection, therefore, the surgeon is essentially a *pus evacuator*. Whatever other attribute he arrogates to himself in this matter is only utter vanity. The writer has on other occasions pointed out these shortcomings of the surgeon in dealing with infection. The patient must still grimly fight out the battle of acute pyogenic infection with no specific help from outside sources. The surgeon must resign himself to supporting the natural defenses of the body during this combat and must continue to restrain his own hand from active interference, lest he do harm.

Affording the patient physical and physiologic rest so far as it can possibly be attained is the most worth while measure which the surgeon can accomplish in acute infections. In an infection of the soft tissues, immobilization of the hand, arm, and trunk in a plaster of Paris spica has proved very effectual in the experience of the author in helping to delimit the spread of the infection. In the presence of

swelling, the force of gravity is probably the most important agent in bringing about its disappearance. Only when signs of abscess formation are present is an incision made. Similarly, in acute osteomyelitis of a long bone, the author's practice has been to immobilize the extremity and the body trunk in plaster with a window over the tender area; when there is evidence of a soft tissue abscess, a small incision is made to permit evacuation of the exudate. The results of this conservative regimen, in the author's hands, have been more satisfactory than those of more frequently practiced energetic surgical intervention.

Such immobilization unfortunately cannot be attained in infections of the lung, the pleura, and the upper portion of the peritoneal cavity.

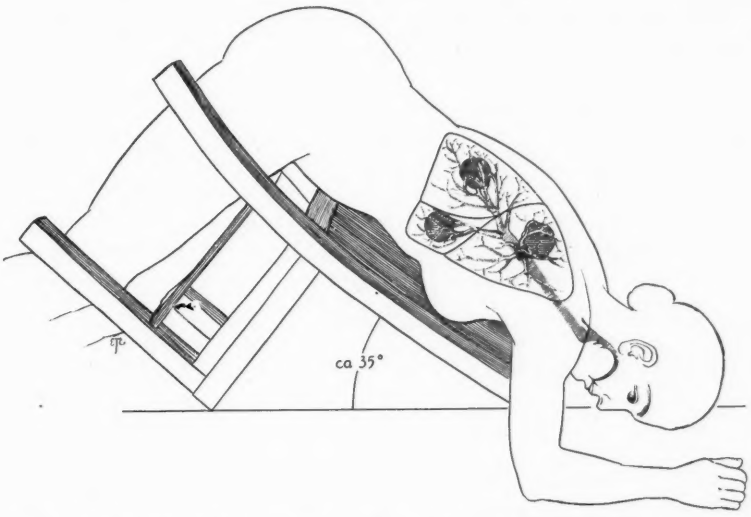

Fig. 3.—The mechanics of postural drainage for an abscess in each of the lobes of the right lung is schematically depicted here. The inclination of the ventral surface of the body with the horizontal plane is about 35° (measured with the protractor 38°)—a fairly steep angle for an ill patient to assume for any length of time. It would appear that a localized pulmonary abscess in the lower lobe communicating with one or more fairly large bronchi would be most favored by the force of gravity in securing satisfactory evacuation. That this method does not meet the requirement of mechanically satisfactory drainage is immediately apparent. It is intermittent, and dependent evacuation can not be maintained for long periods of time. The drainage tract is also too long. That this means suffices to bring about healing in a large number of pulmonary abscesses, despite the handicaps listed above, is well known.

The lungs must expand and deflate twenty-five thousand times or more a day in the process of respiration. The most fundamental principle of absolute rest cannot, therefore, be obeyed by nature in abscess of the lung, or enforced by the surgeon. When, however, evidence of localization of the suppurative process is plain, external drainage of a pulmonary abscess is in order. In discussion of lung abscess at the meeting of the Association for Thoracic Surgeons in 1936, Neuhof

made a plea, well supported by personal experience, for earlier surgical intervention in lung abscess. The present author would suggest a return to those principles which guide and dictate surgical intervention in other abscesses. When irrefragable evidence of localization in a pulmonary abscess is present, surgical drainage should be instituted. Why wait? The only deterrent to operation should be that added short periods of observation reveal unmistakable signs of spontaneous resolution which warrant continuance of the expectant plan. How long a period of time is required for localization of a suppurative process in the lung has not been well defined. Eight to twelve weeks of patient waiting is undoubtedly too long.

SUMMARY

A bloodless method of draining a lung abscess with minimal destruction of lung tissue by employment of graduated trochars with cutting edges combined with the use of the coagulating current of surgical diathermy is described. The hazard of hemorrhage which attends Hilton's method of opening an abscess when applied to the lung and the destruction of considerable lung tissue in the surgery of access by the cautery method are avoided in the technique here described. The limitations of the surgeon in dealing with inflammation are discussed. Earlier external drainage for pulmonary abscess when localization has occurred is urged.

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SURGICAL TREATMENT IN SIXTEEN CASES OF ANTERIOR MEDIASTINAL TERATOID TUMORS: ONE COMPLETE REPORT OF A CASE*

STUART W. HARRINGTON, M.D.
ROCHESTER, MINN.

TERATOID mediastinal tumors are probably of greater interest than any other type of tumor within the thorax because of their congenital origin, the varied symptoms to which they give rise, the clinical course of the disease, which often simulates inflammatory disease, and the difficulties which often are associated with establishing a diagnosis whether from the clinical manifestations or the roentgenologic findings.

In 1933, I reported before this Society eleven cases of mediastinal and intrathoracic teratoma in which I had removed the tumors surgically. I shall add the clinical manifestations and surgical treatment in five additional cases to the general summary of the eleven cases which have been reported previously, making a total of sixteen cases, and shall report in detail one of these cases of which I also shall present a motion picture. The remaining four of the five new cases will be reported in detail in a later paper.

The etiology of teratoid tumors has been the subject of much investigation and speculation. Many hypotheses have been advanced to explain the origin of these growths, but the question of derivation of the tissues of which they are composed has never been definitely answered. I shall not consider in detail the various hypotheses, but shall mention only those that appear most plausible as they influence the terminology used to designate the different types of tumors. The earlier hypotheses were based on the conception that these growths were composed of tegmental structures only, and that they were the result of inclusion of an invaginated portion of the ectoderm at the time of the closure of the primitive wall of the thorax.

The term "dermoid tumors" was given to these growths on the basis of this early view, and most of the earlier cases in the literature were reported under this designation. In many such cases the term is a misnomer as the lesions are of more complex structure than the name indicates. When serial sections of this type of tumor began to be made, their histologic structure became clearer. It was found that many contained tissue derived from the mesoderm and entoderm, and it was impossible to explain the presence of these tissues on a basis of invagination of ectoderm. The hypotheses of origin from the thymic gland, the

*From the Division of Surgery, the Mayo Clinic, Rochester, Minn.

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thyroid gland, the branchial clefts, and the bronchi were then advanced, but these failed to explain the presence of many tissues. Because of the presence in many growths of tissue derived from all of the blastodermal layers, it was thought that fetus in fetu might explain the autogenesis of the majority of these conditions. There are many examples of growths containing fetal tissue, but it is extremely rare for these growths to become so highly developed as to be recognized as a fetus. Certain embryologists claim that the growths are never enclosed within the cavity of the body, and that they should exhibit traces of vertebral segments to prove the presence of metamere structures before they can be considered as bigeminal parasites.

Since the origin of these tumors has not been definitely proved, the terminology should depend on the histologic study of the tissues contained in the growth. Inasmuch as many of the tumors contain tissues derived from all three germinal layers, ectoderm, mesoderm, and entoderm, it is best to group them all under the general term "teratoma" and qualify them according to the type of tissue which predominates in the growth.

In this series of sixteen cases of teratoma, seven were of the dermoid type. In three of these seven, the structures were derived from the ectoderm alone. In the other four cases the structures were mainly derived from the ectoderm and were at first thought to be true dermoid cysts, but later extensive serial sections through the tissue revealed structures derived from all three of the germinal layers, although few structures were derived from the mesoderm and entoderm as compared with those derived from the ectoderm. In six of the sixteen cases the tissue elements were derived from all three of the germinal layers; four of these growths can be considered of the bronchiogenic type; one, of indefinite origin, can be considered diaphragmatic, and the structures of one had attained such a high degree of organoid structure that it was designated as a fetal parasite. The remaining three tumors of the sixteen were malignant; two growths were squamous-cell epithelioma, grade 4, in dermoid types of teratoma, and the other tumor was an adenocarcinoma, grade 3, in a bronchiogenic type of teratoid tumor. This I believe to be a malignant change of an originally benign teratoid tumor.

In fifteen of the sixteen cases the tumor originated in the mediastinum; in six of these fifteen cases the tumor projected into the left thoracic cavity, and in six into the right thoracic cavity. In one case the tumor projected into both thoracic cavities, more markedly on the right than the left. In two cases the tumor was confined to the anterior and superior mediastinum and appeared in the neck. In the remaining case of the sixteen, the tumor apparently originated in the right side of the diaphragm and may have originated from cell inclusion with improper fusion of the septum transversum and pleuroperitoneal membrane at the time of closure of the diaphragm. In fifteen of the cases the tumors were

cystic; in the remaining case the growth was solid; this was the one case in which the tumor was designated as a fetal parasite.

The contents of the cysts were hair and sebaceous material in the seven cases in which the tumors were of the dermoid type. Clear fluid was present in seven cases, and in five of these cholesterol crystals were present. One of the cases in which there was clear fluid in the sac was the case of adenocarcinoma. In the two cases of squamous-cell epithelioma bloody fluid was present. The lining of the fifteen cystic tumors consisted of columnar epithelium in four cases; squamous epithelium in six cases; both columnar epithelium and squamous epithelium in different cystic portions in two cases, and degenerated fibrous tissue with an area of epithelium in two cases of malignancy, and in the one case in which the growth originated in the diaphragm. A great variety of structures was found in the walls of these cystic tumors when serial sections were made. The most common structures were various types of glands; mucous glands were found in six cases; salivary glands in two; sebaceous glands in eleven; sweat glands in nine; cartilage in eight; bone in six; teeth in two; muscle tissue in five; connective and fibrous tissue in nine; lipoid tissue in four; nerve tissue in three; thymic tissue in one; pancreatic tissue in one; and pulmonary tissue in one.

The average age of the patients in this series was thirty-two years; the youngest patient was seventeen years of age, and the oldest, fifty-nine. In thirteen cases the tumor was benign, and in three it had undergone malignant change. The ages of the patients in the three cases in which the growth was malignant were forty-nine, fifty-nine, and twenty-two years, respectively.

Twelve of the patients were women and four were men. Of the three patients whose growths were malignant, one was a man and two were women. On the basis of the total number of cases, the average duration of symptoms was three years and two months. Pain was the chief complaint in eight of the sixteen cases; dyspnea, in four cases, and cough, in two cases; in both of these two cases the expectorated material contained blood and hair at intervals. In the remaining two cases of the sixteen the patients had been operated on previously elsewhere and had draining wounds. In one of these cases the tumor had been partially removed by multiple operations, and in the other exploration had been made.

In reviewing the symptoms in these cases it was found that dyspnea was the most common symptom usually noted on exertion; it was present in twelve cases and was usually associated with pain. The degree of dyspnea depended on the size of the tumor and its site. It was most marked in cases in which a large tumor projected into the thoracic cavity and caused partial collapse of the lung. Pain was the chief complaint and was dependent more on the site of the growth than on its size. It was also the most important symptom in distinguishing

clinically between benign and malignant growths. In cases of malignancy the pain was at first intermittent, then progressively more severe until it was more or less constant. The pain was most severe at night and sedatives were required for relief; in two cases it extended down the arm. In the cases in which the growth was benign, the pain was much milder, usually was localized in the substernal region, occasionally extended along the wall of the thorax, and it was usually believed to be owing to pleurisy. The pain often subsided with rest and conservative treatment.

Cough was the chief complaint in two cases and was part of the complaint in four other cases. In the two cases just mentioned, the attacks of coughing occurred chiefly at night and were associated with expectoration of thick, tenacious mucoid material and hair, and occasionally with moderate hemorrhage from the lung. This is pathognomonic of the presence of a teratoid tumor of the dermoid type which has ruptured into the lung and has produced bronchial fistula; the hemorrhage results from secondary abscess in the lung. Of the four cases mentioned, the cough was of a dry type in two, and was associated with mucoid expectoration in two. It is of interest to note that in one of the cases in which the growth was malignant there was a dry, nonproductive cough, and in the other two there was no cough or expectoration.

Bulging of the wall of the thorax was noted in five cases. In one of the cases in which the growth was malignant bulging was first noted thirty years before I examined the patient. In three of the cases in which the tumor was benign, bulging had been noted respectively five, three, and two years before examination, and in one case in which the growth was benign, it had been noted one year before examination. This latter patient also had noted pulsation of the thoracic wall synchronous with the heart beat three months before admission.

The most common features in these cases were the intermittent character of the subjective symptoms, their gradual progression, and their association with acute respiratory infections, which accounts for the fact that a diagnosis of pleurisy, pleural effusion, pneumonia, or bronchiectasis was made clinically in eight of these cases. In a few cases the diagnosis of teratoid tumor can be made on the basis of the clinical symptoms and the physical condition, but in most cases other methods must be resorted to in order to establish a correct diagnosis. The most important of these is thorough roentgenographic examination of patients who present suggestive symptoms.

The roentgenologic manifestations of teratomas are not as clear cut as those of other types of tumor, and, even after the most exhaustive roentgenologic study, a definite diagnosis cannot be established.[2] Fortunately, it is in this group that the clinical symptoms are often of great aid in assisting in determining the type of tumor present. I believe that one of the main reasons for difficulty in establishing a definite

roentgenologic diagnosis in these cases is that marked inflammatory reaction often is present and produces a change simulating an inflammatory or infiltrating type of lesion in the structures surrounding the growth, often obscuring the definite outline of the tumor. This is particularly true in cases in which the cysts have ruptured into the lung, producing a secondary inflammatory lesion in the lung that may entirely obscure the original lesion. The most common roentgenologic manifestation in the uncomplicated cases is a shadow in the anterior mediastinum; in my experience teratoma is the most common benign tumor situated in this region. The growths usually originate in the anterior mediastinum in the region of the base of the great vessels and upper portion of the pericardium to which they are very adherent, and protrude into one or both thoracic cavities, becoming firmly adherent to the adjacent lung and thoracic wall. The outline of the tumor may be hazy and infiltrating in character when viewed in one plane, but may be of rounded contour when viewed in another. Some tumors, particularly those of the teratoid type, may be cystic and a definite fluid level can be visualized with its surrounding sac. Roentgenoscopic examination of the thorax is important in the diagnosis of these tumors, as most of the growths present a transmitted pulsation owing to their attachment to the pericardium at the base of the great vessels, and great care must be exercised in distinguishing between these lesions and aneurysms of the arch of the aorta or of the descending portion of the aorta. Radiotherapy as a therapeutic test is often of aid in establishing a diagnosis by ruling out the presence of lymphoblastoma, which is one of the most common tumors to be considered in differential diagnosis. Other conditions to be considered in the differential diagnosis are thymoma, substernal goiter, and mediastinal abscess.

SURGICAL TREATMENT

The only treatment that is effectual for anterior mediastinal tumors is their complete surgical removal and this should be accomplished as soon as the diagnosis can be established, regardless of the severity of the symptoms. If these tumors are allowed to remain, there is danger that they will undergo malignant change. If the growth remains benign, the course is usually progressive, and ultimately serious complications and chronic invalidism will ensue, either from pressure on the surrounding vital organs, particularly the heart and lungs, or from inflammatory changes. Not uncommonly infection develops, and the growths rupture into the lung from pressure and are secondarily infected, producing bronchial fistula or secondary abscess which often produces severe hemorrhage from the lungs, and may result fatally. The growths should be removed before these complications have occurred, but unfortunately many patients do not present themselves until serious symptoms or complications have developed.

Much of the advancement that has been made in surgical removal of intrathoracic growths has been accomplished because of marked improvement in the administration of anesthetic agents.[2] The greatest immediate danger in intrapleural operation is open pneumothorax with collapse of the lung. This may produce severe respiratory and circulatory disturbances which may result in sudden death. These dangers have been practically eliminated by the use of intratracheal anesthesia, induced by means of an apparatus by which gas and oxygen are administered under positive pressure. I prefer cyclopropane as the anesthetic agent; the administration of the anesthetic should be in the hands of a skilled anesthetist. In cases in which partial collapse of a lung is required, the lung should be permitted to expand fully every four to five minutes during the course of the operation. A suction pump should be applied to the intratracheal catheter, before it is withdrawn, to remove any mucus that may have accumulated in the trachea. It may be stated that the use of intratracheal, positive pressure anesthesia has been of the same relative importance to the technical problems associated with surgical removal of these growths by transpleural operation as roentgen rays have been to the clinical diagnosis of the lesions.

The chief technical difficulties associated with surgical removal of these growths are as follows: (1) Access is through the bony encasement of the thorax, and a method of approach must be selected that will give the greatest exposure of the tumor with the minimal amount of trauma to the thoracic viscera and thoracic wall. (2) Traction on the important structures in the mediastinum, to which the tumor might be adherent, is an element of danger. (3) Complete reconstruction of the thoracic cage, so as to restore the normal relations of the thoracic viscera and to give the minimal amount of deformity, is advisable.

The methods of approach and types of operative procedure depend, to some extent, on the site of the tumor and on the complications that have occurred. Each case must be considered individually, depending on the indications presented. A few general principles apply to all cases. The most important is early operation and complete removal of the tumor; this can be accomplished in multiple stages, but I prefer to remove the growth in one stage if possible, as the second stage may be more hazardous and difficult than the first. Incomplete removal of the growth may be followed by more serious trouble, and usually will require subsequent operative procedures.

The method of approach may be through the anterior or posterior wall of the thorax, but I prefer the posterior approach, particularly when the tumor projects into the pleural cavity or is adherent to the lung, because much greater exposure can be obtained and the important structures to which the tumor is adherent, usually the heart, the great vessels, and the lungs, can be carefully dissected from the growth under direct vision. Any injury to these structures caused by tumor or opera-

tive procedure can be detected and repaired immediately, and if infection is encountered in the cyst or lungs, drainage can be readily instituted. If the tumor is confined to the anterior or superior mediastinum, I prefer the anterior approach, either splitting the sternum, or resecting the cartilage and turning back the wall of the thorax.

In this series of cases posterior thoracotomy and mediastinotomy was done in ten cases; posterior thoracotomy, in one case; posterior thoracotomy and repair of a defect in the diaphragm, in one, and anterior mediastinotomy in three, in one of which the sternum was split and in the other two cartilages and a portion of the corresponding ribs were resected. In one case combined posterior thoracotomy and anterior mediastinotomy was performed. The tumor was completely removed in fifteen cases, all by operation in one stage. In eleven of these cases, the growth was removed transpleurally, and in four cases, extrapleurally. In six cases it was necessary to cut into the lung to remove the growth, and the tissue was repaired by suture. In the remaining case of the sixteen, the growth was malignant and could be removed only partially.

Indications for draining the thoracic cavity are presented in each case. When there is no infection, or no complication arises in the removal of the tumor, the thoracic cavity should be closed without drainage. If the tumor is infected and the pleural cavity is contaminated, it is usually best to drain the cavity or the mediastinum. I prefer to drain the pleural cavity by the intercostal, closed method. In this series of cases the thoracic cavity was closed in five cases and drained in eight. The mediastinum was drained in three cases.

In practically all cases postoperative effusion develops and usually repeated aspirations are required; in some of these cases empyema ultimately develops and requires drainage. Occasionally a mediastinal abscess or osteomyelitis of the ribs occurs.

The convalescence in seven cases of this series was uncomplicated except for moderate pleural effusion. Five of these cases required one or more aspirations. In five cases empyema developed, requiring drainage with rib resection; in one case mediastinal abscess developed, requiring rib resection for drainage, and in one case osteomyelitis of the ribs developed, necessitating partial removal of three ribs. This accounts for fourteen patients; two did not recover from operation, as will appear presently.

Postoperative care is of the utmost importance. Particular care should be taken to maintain the blood pressure and to relieve any respiratory difficulty. It is usually advisable to give some form of intravenous medication, either in the course of the operation or immediately afterward. If much blood has been lost transfusion of blood should be given; if this is not practicable, infusion of solution of acacia is satis-

factory. Respiratory difficulty is the most serious immediate complication and is best relieved by placing the patient in an oxygen cabinet. This is often a lifesaving procedure, as sufficient oxygen can be obtained to tide the patient over the most critical postoperative period of respiratory embarrassment. In six cases of the series transfusion of blood was given on the operating table, and in seven cases the patients were placed in the oxygen cabinet immediately on leaving the operating room. The period of hospitalization varied from eighteen days to five and a half months.

Fig. 1.—Anteroposterior view showing large tumor filling lower three-fourths of right thoracic cavity and extending above second rib anteriorly, completely collapsing the middle and lower lobes of the right lung, and displacing the heart and mediastinum to the left.

Fourteen patients recovered from the operation. There were two operative deaths, one on the seventh day, from cerebral embolism. This was the patient who had a malignant tumor. One patient died on the fourth day from pneumonia. This was the only death in a case in which the tumor was benign in the entire series and is the case in which combined anterior mediastinal and posterior thoracotomy was required. One patient died six months after operation from malignant disease. Thirteen patients are living, with complete relief of symptoms.

REPORT OF A CASE

A woman, aged fifty-three years, came to the Mayo Clinic, December 2, 1936, because of a tumor of the thorax, which had been discovered in the course of an attack of influenza nine years prior to her admission. For the past fifteen to twenty years she had had repeated attacks of pulmonary trouble, diagnosed as pleurisy, influenza, and pneumonia. Chief symptoms were severe cough with mucopurulent expectoration, dyspnea, and fever. At first the symptoms were mild. The first severe attack had occurred at the time when the tumor was discovered. Thereafter, attacks had been more frequent and severe. For the last attack just prior to the patient's admission, hospitalization of four months had been required. When the

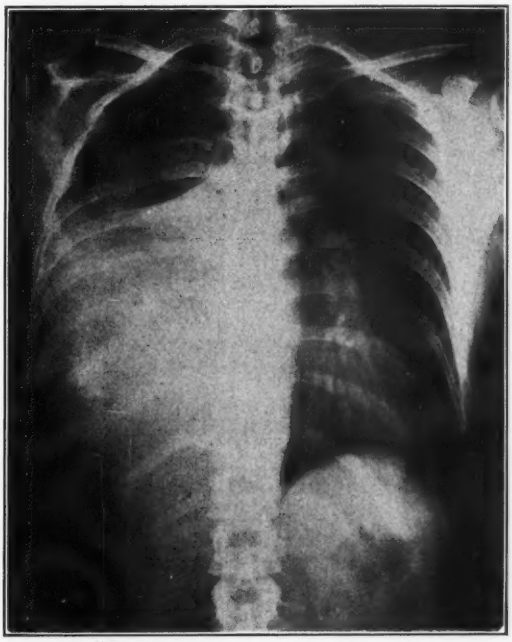

Fig. 2.—Calcified material (5 teeth and bone) in center of the tumor. Roentgenogram made with Potter-Bucky diaphragm.

patient came under my care she was unable to walk more than a block or two because of dyspnea and palpitation of the heart. Cough had been more troublesome since the attack of pneumonia. She had not lost weight and her weight on admission was 107 pounds (48 kg.).

Examination revealed dullness over three-fourths of the right lung and decreased breath and voice sounds. The blood pressure was 130 systolic and 86 diastolic. Urinalysis gave negative results except that a few pus cells were seen. The concentration of hemoglobin was 14.9 gm. per 100 c.c., erythrocytes numbered 4,760,000, and leucocytes 12,700 per cubic millimeter of blood. The Wassermann reaction of the blood was negative. Roentgenograms of the thorax revealed a large tumor filling the lower three-fourths of the right thoracic cavity, extending above the second rib anteriorly, completely collapsing the middle and lower lobes of the right lung, and displacing the heart and mediastinum to the left. A roentgenogram made with

the Bucky diaphragm gave evidence of calcified material in the center of the tumor (five teeth and bone). The lateral view revealed that there was a tumor filling the entire lower part of the thoracic cavity, extending more anteriorly than posteriorly. Its upper anterior attachment extended to the middle of the manubrium (Figs. 1, 2, and 3).

A clinical diagnosis was made of right anterior mediastinal teratoma.

December 26, the tumor was completely removed by a transpleural operation in one stage, with the patient under intratracheal anesthesia with cyclopropane. Right posterior mediastinotomy was performed by removing segments of the seventh and eighth ribs, and the pleural cavity was entered through the posterior periosteum of the seventh rib. On exploring the pleural cavity a large tumor was found. It was

Fig. 3.—Lateral view showing a tumor filling the entire lower part of the thoracic cavity, extending more anteriorly than posteriorly. Its upper anterior attachment extends to the middle of the manubrium. Calcified material in center of tumor.

yellowish, filled the entire posterior portion of the thorax, and extended into the right pleural cavity, causing almost complete collapse of the lung. The tumor had perforated into the lung in several places, and the entire middle and lower lobes and the lower portion of the upper lobe were collapsed. The tumor was firmly adherent to the entire median and lateral aspects of the right lung, into which it had ruptured in several places, and also it was adherent to the thoracic wall. Some difficulty was encountered in separating the tumor from the thoracic wall, but there was greater difficulty in separating it from the lung and particularly from the pericardium and great vessels, where it was most adherent and seemed to have had its origin. It was necessary to remove part of the outer layer of the pericardial sac with the tumor, but the inner layer of the pericardium was not divided. The lung was sutured in four places, where there were small bronchial fistulas as the result of the

tumor rupturing into the lung. The tumor was opened into in several places in the course of its removal and large quantities of mucoid and sebaceous material and hair escaped. The entire wall of the sac was removed, the many small fistulas in the lung were repaired and the pleural cavity was drained with a No. 26 French catheter inserted through the periosteum of the tenth rib after a portion of the rib had been removed. The lung was inflated, and air was aspirated from the pleural cavity before closure. The posterolateral incision was completely closed with inter-

Fig. 4.—Operation for removal of the tumor.

rupted and continuous sutures. A transfusion of citrated blood was given, and the patient was immediately placed in the oxygen chamber (Fig. 4).

Microscopic examination of the tumor disclosed a multilocular dermoid cyst. It measured about 27 × 20 × 10 cm., and weighed 1,820 gm. after most of the contents of the cyst had been removed. The cyst contained hair, five teeth, sebaceous glands, sweat glands (part of which were cystic), and also a small amount of bone. Some of the cavities were lined with squamous epithelium and contained sebaceous material, while other cavities were lined with columnar epithelium and contained a jellylike substance. There was no evidence of malignant neoplasia.

At completion of the operation the woman's pulse rate was 120 per minute and her blood pressures 80 and 40. A second blood transfusion was given, and twelve hours after operation the pulse rate was 100 and her blood pressures 110 and 60. Immediate convalescence was uneventful. On the second day the temperature was 101° F. and the pulse rate 100. On the fourth day, the temperature was normal and the pulse rate was 90; these remained about the same until the twenty-first day, when the temperature and pulse rate increased. On the twenty-second day the temperature was 102° F. and the pulse rate 120. Drainage from the intercostal drainage tube had ceased for forty-eight hours, and it was concluded that the increase in

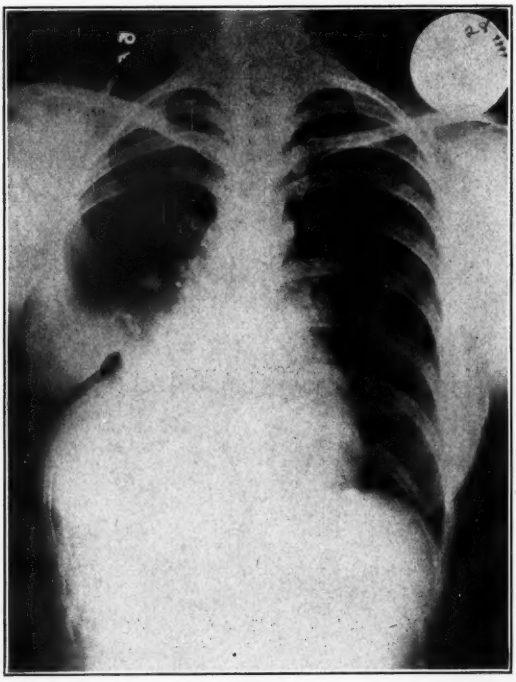

Fig. 5.—Roentgenographic appearance four months after operation. Heart and mediastinum in normal position. Left lung negative. Partial expansion of right lung evident in upper and middle lobes.

the pulse rate and temperature were owing to encapsulated empyema. The patient was taken to the operating room, and the anterior portion of the posterolateral incision was opened. Encapsulated empyema was encountered in the anterior portion of the cavity which had been occupied by the tumor. This was cleared by open drainage. There were many small bronchial fistulas in this pocket where the tumor had ruptured into the lung. The temperature and pulse rate gradually dropped to normal on the seventh day following the open drainage. This anterior mediastinal empyema cavity has gradually become reduced in size until it is practically obliterated. The bronchial fistulas are entirely healed. The woman has gained 18 pounds (8 kg.) and has no respiratory symptoms. Roentgenograms disclose that the right lung is about two-thirds expanded and otherwise normal (Fig. 5).

This case is of interest because of the long duration of the symptoms and the extensive destruction which the tumor had caused in the lower and middle lobes of the right lung, into which there were many perforations. Although destruction of the lung had been great, there apparently was no residual infection in the lung after removal of the tumor.

The most important clinical symptom in this case was dyspnea associated with pain in the right side of the thorax. The pain had become so severe as practically to incapacitate the patient. The long duration of symptoms and the injury which this tumor produced in the surrounding structures in the thorax were responsible for the long convalescence.

SUMMARY AND CONCLUSION

The clinical symptoms, surgical treatment, histologic findings, and operative results in sixteen cases of mediastinal and intrathoracic teratoma are summarized. One case is reported in detail.

The most important consideration in the surgical treatment is early recognition of the tumor and its immediate surgical removal, regardless of the severity of symptoms caused by it. Delayed operative removal may result in grave complications, such as malignant change or infection in the growth; these increase the magnitude and risk of the operative procedure.

The technique of operative removal of these growths depends on the indications in each case. The posterior method of approach, when possible, is preferred. The tumor must be removed completely; operation in one stage is preferred. The surgical risk is not great. In this series of sixteen cases there were two operative deaths.

The results are good in cases in which the tumors are benign; cure is effected if the growth is removed entirely.

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DISCUSSION

DR. EVARTS GRAHAM, St. Louis, Mo.—I am sure we all admire this beautiful presentation of Dr. Harrington; also the way in which he removed a very large tumor. I should like, first of all, to compliment him upon his splendid results. I should also like to reemphasize the statement which he made about the necessity of operation on all of these teratoid tumors as soon as they are diagnosed. There isn't any question that these tumors do become malignant. One can never tell when malignancy will occur.

An experience with a small boy, seven years old, some years ago, has convinced me of the necessity for immediate operation. He had a large teratoma of the mediastinum which I removed, but he came back three months later with a recurrence

filling up his entire thorax. This was an adenocarcinoma at that early age in life. He died subsequently of generalized metastases.

I was interested in Dr. Harrington's presentation of the posterior approach. In an experience with twelve dermoid or teratoid tumors in the mediastinum, I have found that it is not necessary, as a rule, to make a posterior approach. The advantage of an anterior approach is chiefly one of cosmetic result. In a female patient, particularly an adult female, if one uses an anterior approach, it is possible to make the incision under the fold of the breast, remove no ribs whatever, merely divide the costal cartilages to get thoroughly adequate exposure, and when one is through with the operation and the wound is healed, it is impossible for anyone to tell that the patient has ever been operated upon, a feature which I think has certain advantages. Through the anterior approach, however, I enter the pleural cavity freely on the side toward which the tumor projects.

In seven of these cases of teratoid tumor I have been able to remove the tumor without any mortality. In five other cases, which were malignant, it was found impossible to remove the tumor and only biopsy material was removed.

I think the location of the tumor should make a good deal of difference as to the method of approach. If the tumor is purely in the anterior mediastinum, I think certainly it can be removed with sufficient satisfaction and ease through an anterior approach, this method of which I have just spoken, which will produce ideal cosmetic results. If, however, the tumor is purely in the posterior mediastinum, then I believe a posterior approach will give better exposure.

In this very large tumor which Dr. Harrington showed us, I can see the desirability of removing two ribs, perhaps. Ordinarily, however, I do not think it is necessary to remove any ribs whatever in removing these tumors, at least if they are of ordinary size.

In our own experience, the percentage of malignancy of these tumors has been considerably higher (41.6 per cent) than in the experience of Dr. Harrington. This merely serves to emphasize again the point which he is endeavoring to make, that one should not regard these tumors as forever benign, and if they do not happen to be producing symptoms, to dismiss the patient by saying, "Well, you have a benign tumor and you need not fear it, the worst it can do, probably, is merely to make pressure symptoms," because there is a very strong tendency for these tumors to become malignant. None of these tumors should ever be regarded as benign; they should always be regarded as potentially malignant, and operation should be advised at once, even if the patient is a small child.

DR. LEO ELOESSER, San Francisco, Calif.—If I may allow myself a few remarks: Chance would have it that within the last two years I have seen three teratomas. I think that ordinarily an intercostal approach, as shown by Dr. Harrington, gives good access, and this was also emphasized by Heuer in an extensive paper.

It is futile to try to work entirely anteriorly and to confine one's self to the mediastinum in an endeavor to keep out of the pleural cavity; one soon enters the pleural cavity anyway. I don't suppose you meant to do an extrapleural approach.

DR. GRAHAM.—Oh, no. I approve very heartily of Dr. Harrington's suggestion of always going through the pleura, but I merely like to make an anterior approach.

DR. ELOESSER.—Two little points as to diagnosis. If one can see, as Dr. Harrington showed, calcifications that can be interpreted either as bones or teeth, the diagnosis is established therewith. It is also fairly well established, although it is possible that such a tumor may be a pure dermoid, if the patient spits out hair.

These three patients were lucky enough to survive.

The difficulties are considerable, and I should like to express the appreciation of everybody here for Dr. Harrington's beautiful work.

The difficulties are in part occasioned, probably, by congenital anomalies of the vascular tree and the bronchial tree, which have to do with the development of these tumors; when one begins to develop the pedicle, one is likely to encounter unforeseen difficulties owing to anatomic anomalies of the pulmonary hilum.

DR. STUART W. HARRINGTON, Rochester, Minn.—I am very grateful for this discussion. I am particularly pleased that Dr. Graham has emphasized the possibility of malignancy occurring in these teratoid tumors; whether the malignancy is primary or secondary is difficult to determine, but it is probable that it is a secondary malignant change occurring in a primary benign tumor. The fact that these tumors do become malignant is one of the most important indications for early operations. Unfortunately, many of these patients who are found to have teratoid tumors are kept under observation for long periods of time.

It has been my experience that other types of intrathoracic tumors may become malignant, particularly the neurofibroma type of tumor, which in my experience has been the most common tumor within the thoracic cage. I believe that all tumors that occur within the thorax must be considered potentially malignant.

I agree entirely with Dr. Graham in his discussion of the method of approach, that it must be individualized in each individual case. I prefer the posterior approach for these anterior mediastinal tumors, except in those cases in which the tumor has ruptured forming a mediastinal abscess or has ruptured into the lung anteriorly.

I appreciate very much the discussion, and I would like again to emphasize that surgical treatment of these tumors should be done early, that the tumor should be entirely removed in one operation if possible, and that the methods and details of surgical technique must depend on the indications of each individual case.

SITUS INVERSUS, SINUSITIS, BRONCHIECTASIS*

A Report of Five Cases, Including Frequency Statistics

Ralph Adams, M.D., and Edward D. Churchill, M.D.
Boston, Mass.

THE Thoracic Clinic of the Massachusetts General Hospital recently has seen five cases with the interesting findings of complete transposition of the viscera, bronchiectasis, and disease of the upper accessory air passages. They are placed on record because of rarity, speculation they arouse concerning the congenital nature of certain cases of bronchiectasis, and evaluation of the effect of sinusitis on development of bronchiectasis. The literature is reviewed because we have been unable to find any report of this pathologic constellation written in the English language.

Siewert[1] reported the first case in 1904. A twenty-one-year-old male started coughing within a month after birth, and this persisted all his life. It was accompanied by frequent attacks of vomiting until the age of ten years, and thereafter by large quantities of purulent sputum. On examination there were noted: septal deviation, hypertrophied nasal and nasopharyngeal mucosa, situs inversus, tympany beneath left clavicle with cavernous amphoric breathing, and diffuse râles. The x-ray confirmed situs inversus.

Oeri[2] reported the second case in 1909.

Guenther,[3] in 1923, reported a case of situs inversus and bronchiectasis of the left upper lobe in a nineteen-year-old girl. Her sister also had situs inversus and a "bronchial catarrh." Two other siblings had no "bronchial" history. He gave the incidence of situs inversus as 5 in 63,000 cases, or 0.0079 per cent, by clinical examination; as 3 in 22,000 cases discovered at postmortem. His conclusions were that situs inversus is a constitutional anomaly, which may or may not be associated with other anomalies.

Kartagener[4] became keenly interested in the subject, and in 1933 reported 4 cases illustrating the triad of findings, which sometimes since have been referred to as the Kartagener syndrome. He thought that predominant involvement of any one lobe could not be determined, and concluded that bronchiectasis in combination with situs inversus lends support to Sauerbruch's contention that 80 per cent of cases of bronchiectasis are congenital. Some statistics were quoted on frequency: among 8,000 hospital admissions a year, 0 to 3 cases of situs inversus were seen, 20 to 30 new cases of bronchiectasis. He believed the general

*From the Thoracic Clinic of The Massachusetts General Hospital.
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autopsy average to be about 1 in 5,000 cases. Of comparative interest are 501 cases of bronchiectasis in 34,000 autopsies quoted from Frank.

Nussel and Helbach[5] reported 2 cases in 1934, and discussed the etiologic theories. They believed that situs inversus is one of the rare anomalies, but not a deformity; that it may imply an inherent predisposition to bronchiectasis; that beyond this statement, no conclusion is justified.

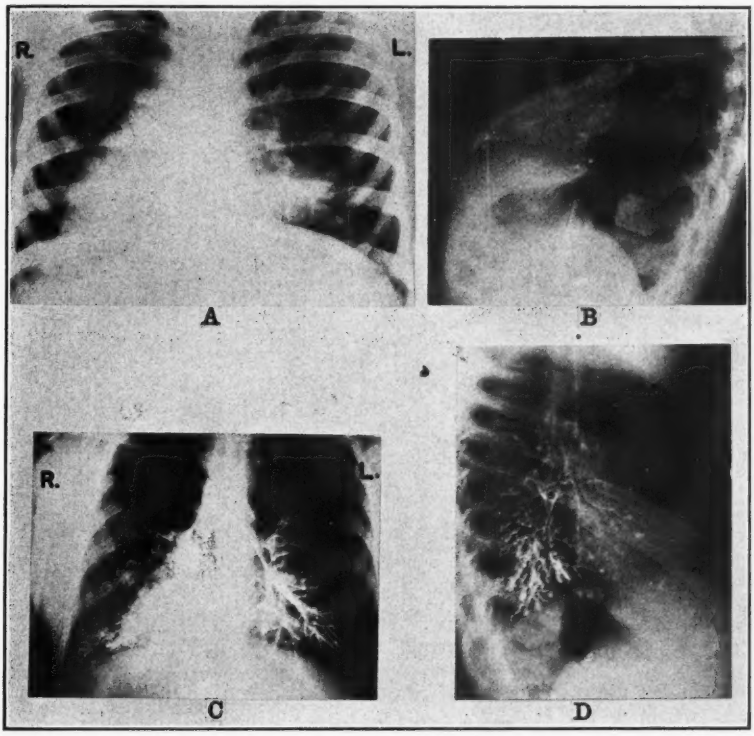

Fig. 1.—*A*, Posterior-anterior view showing heart on right, dullness and striations at both bases; *B*, right lateral view showing patchlike density within heart shadow; *C*, and *D*, posterior-anterior and right lateral views after lipiodol injection, showing bronchiectasis of right lower and left middle lobes.

Kartagener and Horlacher[6] reported 6 additional cases in 1935. Thirty cases of situs inversus were encountered while reviewing the records from which these 6 cases were obtained.

Later in the same year, Kartagener reported his eleventh case. He saw in these cases more than a coincidental combination. The sequel of situs inversus, nasal infection, and bronchiectasis was explained, in his mind, on a common factor; namely, an anomaly, and therefore the bronchiectases were congenital.

Also in 1935, Behrman[7] reported the interesting case history of a twenty-one-year-old male with a family history of tuberculosis. There were attacks of pneumonia at ages of twelve and sixteen years. Following the second attack, constant cough and foul sputum developed. At eighteen years of age he was proved to have enlarged adenoids, deviated nasal septum, left nasal polyps, bilateral otitis media, and tuberculosis of right lung. X-ray films demonstrated situs inversus, dullness throughout the right lung field with many confluent ring shadows of diminished density. At the left base there were increased striations with ring shadows. The patient was believed to have bronchiectasis acquired after the pneumonia and made worse by the tuberculous infection. No evidence was found in favor of the congenital theory of origin in this case.

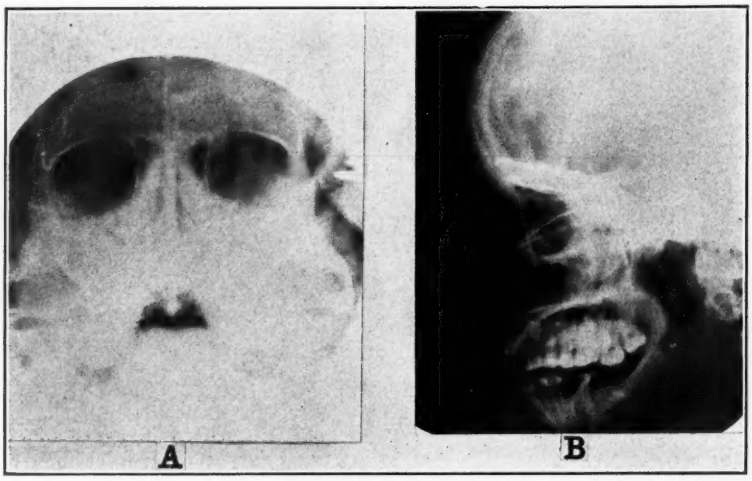

Fig. 2.—*A*, and *B*, Marked pansinusitis.

Kautzky,[8] in the course of an excellent paper on the etiology of bronchiectasis, mentioned 4 cases of situs inversus, 1 of which had bronchiectasis in the right lower lobe. He suspected, also, that this combination is more frequent than can be explained by the laws of chance.

CASES

There have been 23 cases of situs inversus diagnosed in the Massachusetts General Hospital since 1886. Five of these had also bronchiectasis and disease of the accessory air passages.

CASE 1.*—(Figs. 1 and 2.) A nine-year-old girl (S. H.) constantly had an obstructed nose and was a mouth breather. She was essentially well, however, until the age of four years, when she had measles and whooping cough. Following these

*Reported as case by Churchill, E. D.: Lobectomy and Pneumonectomy in Bronchiectasis and Cystic Disease, J. THORACIC SURG. 6: 286, 1937.

illnesses an increasingly productive cough appeared. Between the ages of five and six years, the sputum became profuse, fetid, and occasionally blood streaked. She spent eighteen months in another hospital without any real relief. At the age of eight years she had scarlet fever, complicated by pneumonia and otitis media. Following that illness, there occurred repeated attacks of fever, chills, and drenching night sweats. The sputum averaged one pint daily for the six months before admission and was frequently blood streaked.

On examination by the Thoracic Clinic and other consultants, she was thought to have bronchiectasis of the left lower and right middle lobes. There was slight daily fever and a leucocytosis of 15,000. The sputum contained no tubercle bacilli. The X-Ray Department, on plain and lipiodol films, made the diagnosis of bronchiectasis, left lower lobe and right middle lobe. A bilateral lobectomy in stages was outlined for treatment.

The left chest was opened expecting to resect the left lower lobe. To our amazement, the right lung was exposed. Tactics were changed and the bronchiectatic middle lobe was resected.

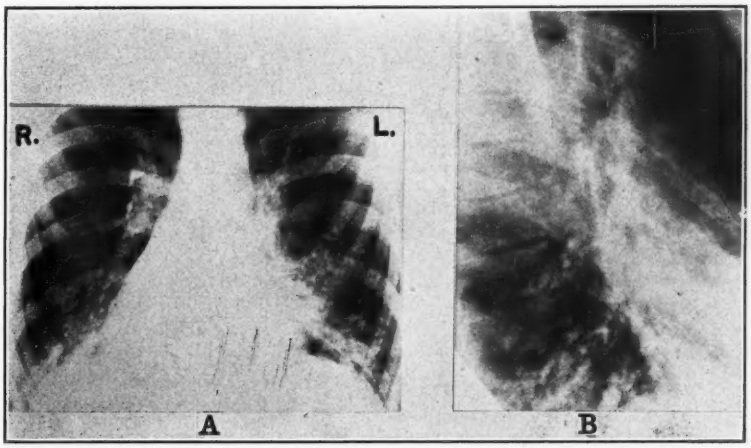

Fig. 3.—*A* and *B*, Posterior-anterior and right lateral views, showing transposed viscera and extensive bilateral bronchiectasis.

On pathologic examination, the resected middle lobe was completely atelectatic and made up practically entirely of large, dilated, thickened bronchi averaging 5 to 7 mm. in diameter.

At a second operation, the bronchiectatic left lower lobe was removed from the right hemithorax. Sinus films four months and nine months postoperatively have shown pansinusitis.

CASE 2.—(Fig. 3.) A twenty-two-year-old male (D. D.) considered himself healthy, without respiratory tract disease. He had mumps, diphtheria, and an operation for the removal of tonsils and adenoids when a small child. A very mild attack of influenza occurred at the age of ten years. The only variations from perfect health, which he recalled, were sore throats for three days thrice yearly, for the past ten years. Two years before admission there was an insidious onset of cough and expectoration which increased to a severe cough with expectoration of one-half cup of sputum daily.

On examination there were impaired resonance, diminished breath sounds, and crackling râles throughout the lower halves of both lung areas. Situs inversus was thought to be complete. A consultant found bilateral nasal obstruction due to

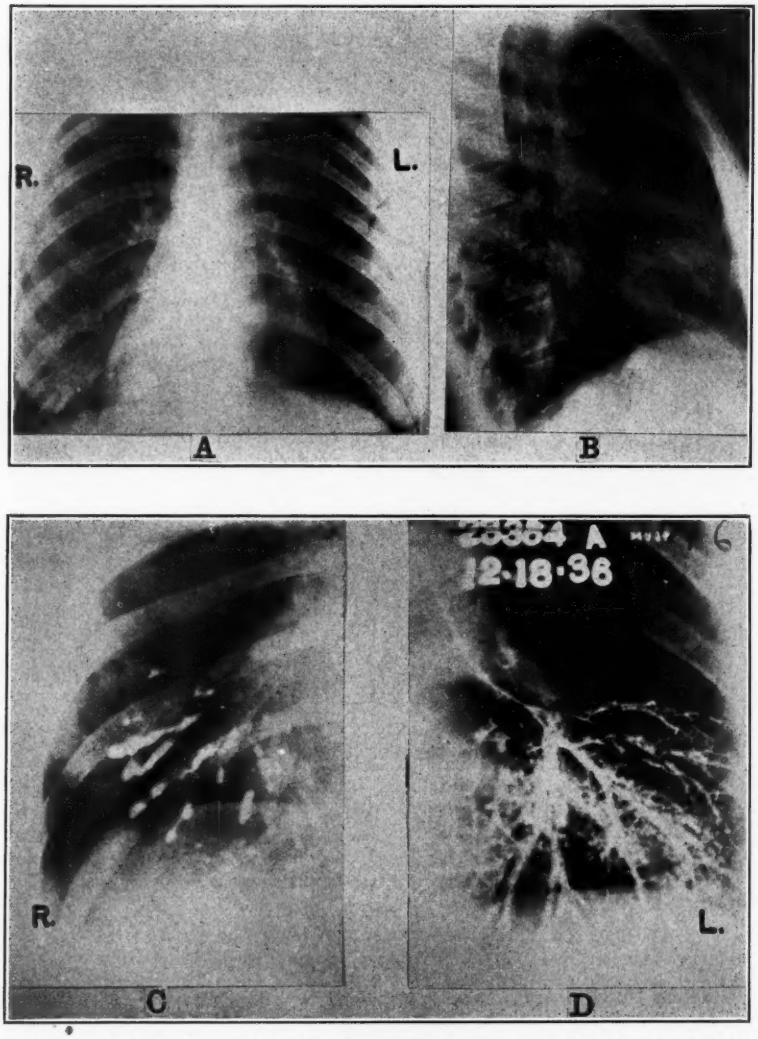

Fig. 4.—*A*, Posterior-anterior view showing transposition, mottled density at right base, increased linear striations in left cardiophrenic angle; *B*, the area of dullness lies posteriorly in the right lateral view; *C* and *D*, "spot films" after lipiodol injection, showing saccular bronchiectasis of right lower lobe, slight cylindrical dilatation of left lower lobe bronchi.

polypoid thickening of the membranes and pus in both ethmoids. Sinus films confirmed the infection of the ethmoids, and in addition showed dullness of the antra. The frontal sinuses were underdeveloped.

Chest films showed complete situs inversus, extensive bronchiectasis, emphysema, and probably pulmonary fibrosis. There was cyanosis on exertion and diminished vital capacity (2,250 c.c.).

CASE 3.—(Figs. 4 and 5.) A twenty-three-year-old female (J. F.) had a cough productive of abundant sputum from earliest childhood recollection. At the age of nine years she was studied in this hospital. A diagnosis of complete situs inversus and chronic bronchitis were made at that time.

At the age of twenty-one years the symptoms became much worse following a severe "cold" and septic sore throat. She experienced intermittent stabbing pains across the right anterior chest for a year before admission and suffered from headaches across the eyes for ten months. A single hemoptysis occurred six weeks before entry. Easy fatigue and the physical inconveniences of her disease adversely affected her occupation as lady's maid.

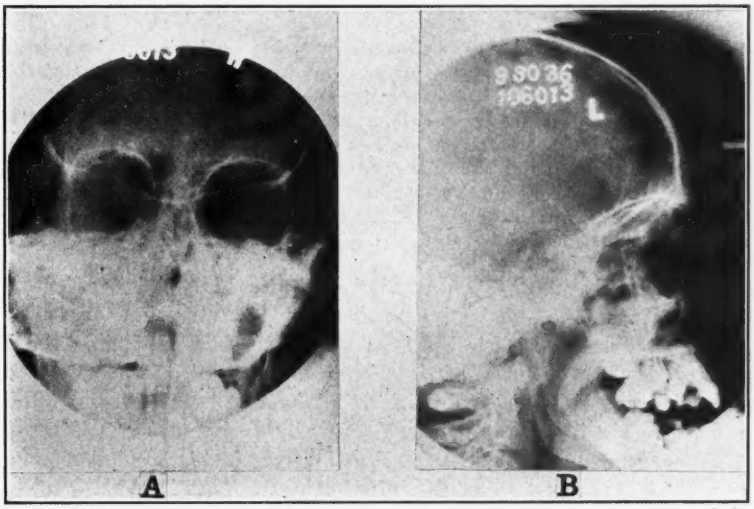

Fig. 5.—*A* and *B*, Dullness in both antra, underdeveloped frontal sinus.

She had whooping cough, chickenpox, and influenza at the age of five, but insisted that she had a productive cough before these diseases. No history of pneumonia was recorded.

On examination, she was found to have situs inversus, poor chest expansion, bubbling râles over both lower lung fields, mostly on the right. Nose and throat examination showed large nasal polyps on both sides, blocking the airways, and bathed by a purulent discharge. X-ray films showed situs inversus, bronchiectasis of the right lower lobe, slight bronchiectasis of the left middle lobe confirmed by lipiodol injection. There was marked clubbing of both antra. Lobectomy was advised after treatment of the antral disease.

CASE 4.—A twenty-eight-year-old, colored female (F. P.) had measles, chickenpox, mumps, and whooping cough in childhood, and right-sided pneumonia at the age of thirteen years. There were no other respiratory symptoms until the age of twenty years, when for five months she had a chronic cough, productive of copious and occasionally blood-streaked sputum. Nose and throat examination revealed enlarged adenoids, diseased tonsils, and hypertrophied polypoid middle turbinates.

A provisional diagnosis of bronchiectasis at the right base also was made. The tonsils and adenoids were removed, but the cough and sputum continued, although decreased. Six months prior to entry, her symptoms became exaggerated and accompanied by frequent slight hemoptyses.

She was admitted seven days after the onset of pneumonia. On examination, she was sick, emaciated, and had a temperature of 101° F. There was situs inversus. Dullness, amphoric breath sounds, and crepitant râles were found at the right base, where tactile fremitus was increased. The sputum showed no tubercle bacilli.

X-ray confirmed complete transposition of viscera. After the acute infection had subsided, right lower lobe bronchiectasis was proved by lipiodol injection. Lobectomy was advised and refused.

CASE 5.—A twenty-two-year-old male (P. L.) had a chronic cough since babyhood, without history of antecedent infection. As long as he could remember, he had been raising four to five ounces of thick, green, foul sputum daily. Throughout life, also, he experienced almost constant anterior and posterior mucoid nasal discharge. The sense of smell was poor, and he was slightly deaf. His scholastic record was poor. Three operations had been done for resection of nasal polyps. Functionally, the patient considered himself to be in perfect health.

Examination and diagnostic studies revealed slight deafness, sclerosis of the mastoid cells, underdeveloped frontal sinuses, sinusitis, nasal polyps, situs inversus, cylindrical bronchiectasis of both lower lobes and the left middle lobe. There were no saccular dilatations. Postural drainage was instituted to be followed by bronchoscopic drainage.

DISCUSSION

There have been 232,112 cases admitted to the Massachusetts General Hospital since 1886, deducting readmissions. In the same period, a diagnosis of bronchiectasis has been made 712 times, including the 5 just cited. The diagnosis of situs inversus is recorded in 23 patients. The incidence of bronchiectasis in the 23 cases of situs inversus is 21.7 per cent. The incidence of bronchiectasis in the hospital population is 0.306 per cent. The incidence of situs inversus in the hospital population is 0.002 per cent. One case of situs inversus has been recorded in more than 8,000 autopsies.

The figures for bronchiectasis by no means represent the incidence in the general population as the hospital admissions show the effect of selection. Two hundred and forty-six cases of bronchiectasis, or 33 per cent of the total number, have been admitted since 1932, when the interest of the Thoracic Clinic in the disease first began to be widely known. Also, 4 of the 5 cases presenting both situs inversus and bronchiectasis have entered within four years.

The third and fifth case histories suggest that the bronchiectasis may have been truly congenital. Ample opportunity for the disease to have been acquired is obvious in the other 3. Disease of the upper air passages existed in all.

As over 90 per cent of all cases of bronchiectasis have symptoms or signs of infection of the accessory nasal sinuses, little emphasis can be placed upon the coincidence of these two components of Kartagener's triad. Although the hypothesis that sinusitis precedes and causes

bronchiectasis has been a popular one, we have personally been unable to subscribe to this view except in occasional instances. It is just as rational to consider the bronchiectasis primary and the sinusitis secondary or both conditions due to a common underlying element. In point of fact, the very existence of this so-called triad lends support to this argument. No figures are available to indicate the frequency with which bronchiectasis demonstrable by lipiodol injection occurs in an unselected group of patients with chronic sinus infection. It is our impression, however, that it would in no manner approach the regularity with which the association of the two is found in the cases recorded here and cited above from the literature.

In our opinion, therefore, the really startling coincidence of this syndrome is the association of bronchiectasis with situs inversus. Given the bronchiectasis, the sinusitis is a logical and expected corollary.

George Fisher[9] wrote rationally about situs inversus in 1887. Congenital, or true transposition of viscera, is a variation from the normal type of animal organization. There is not merely a change of location of the organs and their relations to each other, but there is also a reversal in the relative position of every part of the transposed organs themselves. They are evolved and developed in the embryo right or left, as are the hands and feet, and other parts of the body possessing right and left asymmetry. Situs inversus pertains to the science of teratology, and teratology is essentially a subdivision or phase of normal embryology. Almost all the malformations described by teratologists are the result of arrest of development at some stage of embryonic growth. It is impossible to tell what disturbing influence tilts the balance of the nonsymmetrical organism into the opposite direction, or how the cause of arrest operates.

After making these prophetic statements, amazing in the light of subsequent knowledge, Fisher favorably discussed theories of retrocessive evolution and fetal changes of position, which since have been disproved as ingenious but untenable hypotheses.

Mall,[10] in 1908, considered monsters in great detail and reported experimental work attempting to prove deformity due to an interference with nutrition and growth rate. He also pointed out the natural division of monsters into two groups: (1) those in which the causal elements are in the germ plasm, and therefore inherited; and (2) those due to external influences acting upon the egg after it is fertilized. Chemical salts and variations in oxygen tension were some of the experimental methods used.

Stockard,[11] in 1921, published further fundamental work on developmental rate and structural expression. A given animal species passes through its embryonic stages at a specific rate of development, probably dependent upon the rate of oxidation in the protoplasm of the species. This rate varies within certain normal limits. Should variations ex-

tend beyond these limits, the developmental result frequently is modified and distorted. In most forms the rate of development is continuous. This mode may be experimentally changed into a discontinuous one by either lowering the temperature, and thereby reducing the rate of oxidation, or by directly cutting off the supply of oxygen. The effects of such interruptions on development depend upon the stage at which it is introduced. The critical stages characteristically are those in which marked inequalities in rate of cellular proliferation are taking place in different parts of the embryo.

Nearly any recognized deformity, other than those resulting from germinal variations or mutations, may be induced by lowering the temperature and thus modifying the developmental rate. From Fundulus eggs it was possible to induce a given type of defect by a great variety of experimental conditions. Conversely, all varieties of defects could be induced by subjecting the embryos to one and the same experimental modification of the environment.

The following propositions were formulated[12] from Stockard's work: The end products of development differ from one another in degree only; thus the monster is the exaggeration of the extreme deviation or deformity, and the latter is an exaggeration of the minor aberration. All types of monster, double as well as single, may be caused by one and the same experimental method. Any one type of monstrosity, such as cyclopia, may be produced by a variety of experimental methods. The primary action of all experimentally induced environmental changes is to inhibit the rate of development. The type of monster produced depends upon the time of growth at which inhibition is applied. The part or organ developing at the most rapid rate is most inhibited and is, therefore, most modified in further development.

Inhibition in the pregastrula stage usually leads to twinning. The outstanding mammalian example of twinning occurs in the nine-banded armadillo, which normally produces four or eight embryos from a single egg. The egg lies unimplanted in the uterus for a considerable period during the pregastrula stage, thereby being subjected to a serious oxygen lack. Polyembryony occurs because of the resulting inhibition of the developmental rate. There is a time in every fertilized egg of differentiation into organ rudiments. Before this time, certain experimental alterations are possible.

Newman,[13] in 1923, while making a study of aberrations at various stages of development following exposure of the echinoderm, *Patiria miniata,* to low temperatures, made discoveries of importance to this discussion. It was found and repeatedly proved that subjection of *Patiria* blastulae to low temperatures brought about a considerable increase in the percentage of larvae showing reversed or right-handed asymmetry.

The normal embryonic and larval periods of Patiria were examined, paying chief attention to the origin and development of asymmetry. A statistical study of large numbers of larvae after the posterior celom was fully formed showed an average incidence of 8 per cent with reversed or right-handed asymmetry, 92 per cent with left. In every culture observed, the right-handed individuals maintained their reversed asymmetry, and developed on the average as normally as did the more typical left-handed larvae.

It was found by preliminary trials that the blastula stage is the one best adapted for the experimental induction of reversed asymmetry. Larvae blastulae then were placed in environments identical to those of the first study and divided into lots. One lot was kept as a control; other lots were subjected to temperatures of 2° to 3° C. for one, two, and three hours, respectively. The iced lots showed a significant increase of symmetry reversal over the controls; 27 per cent of reversed larvae, as compared with 12 per cent for the controls. The experiments included forms exhibiting bilaterality, which is harder to induce than straight reversal. A large percentage of the experimentally reversed larvae were smaller and less advanced than the controls.

Newman concluded: "It may be said that symmetry reversal, and that particular phase of it which we may call induced bilaterality, are merely some of the specific effects resulting from arresting the growth of larvae at the blastula stage. If the arrest takes place much earlier or much later than the blastula stage, other expressions of differential inhibition prevail, and there is no evidence of symmetry reversal. If eggs are iced during early cleavage, or even before cleavage, the particular response is twinning, while icing at other times gives equally striking but different results."

Driesch[12] had found, in 1906, that bilaterality was definitely established at the eight-cell stage, and that the first cleavage plane coincides with the sagittal plane of the larva. In most twins produced from physiologically isolated blastomeres of this stage, the rate of development of the two larvae is different, one always being ahead. These data indicate that expression of asymmetry is traceable to a very early embryonic stage and is probably present in the unsegmented egg. It is believed to be due to an inequality of metabolic rate between the antimeric halves of the egg or embryo, so that one side develops more rapidly than the other and controls the symmetry. This difference, being quantitative, is subject to inhibition, and all the structures that should appear on the left, or superior side, may under proper conditions appear on the right, or inferior, side.

The pitfalls of attempting human correlations from experiments in lower forms are well recognized. However, the work quoted permits the formulation of certain hypotheses.

There are numerous clinical observations that a person with situs inversus may be a normal person.[14] Theoretically, this individual is transposed as a result of an ascendent right-handed tendency in the preblastomere stage, probably in the unsegmented egg. That is, he is a mutant. In *Patiria* experiments, the small percentage of inverted yet functionally normal individuals in the control groups support this thesis. A person with situs inversus accompanied by other stigmas of maldevelopment, on the other hand, might be considered one in whom reversal has occurred as a result of environmental factors inhibiting development at a critical period. Also theoretically, by a variation in time and duration of inhibition, this individual might have developed as one of monozygotic twins, the reversed half of Siamese twins, a double-headed monster, or have included within his uninverted organs a teratoma. The important point is that the inferior tendency gained ascendency at a critical period and stigmas of subnormalcy resulted.

In summary, embryologic data make the hypothesis tenable that there may be two types of individuals with transposition of viscera. First, completely normal mutants, and second, true monsters in whom other stigmas of maldevelopment may be anticipated. The natural inference is that the bronchiectasis in these cases is to be regarded as a stigma of maldevelopment.

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DISCUSSION

DR. EVARTS A. GRAHAM, St. Louis, Mo.—I should very much like to ask Dr. Churchill if these are cases of bronchiectasis, or cases of congenital cystic disease of the lung. I should like him to explain a little more clearly to us his definition of bronchiectasis.

DR. LEO ELOESSER, San Francisco, Calif.—There is one more mathematical juggle that Dr. Churchill might have gone through, which is also dependent upon Dr. Graham's question; dependent namely upon whether one considers bronchiectasis a condition or a disease. If one considers that bronchiectasis is manifest only when it becomes infected, then it is entirely likely that many of these situs inversus bear symptomless uninfected bronchiectasis. Could we gather a number of patients with

situs inversus and inject their bronchi with lipiodol, we might find larger percentages of bronchiectasis than Dr. Churchill has. The uninfected ones are probably symptomless: the clinically manifest ones are due to the superadded factor which, as he states, is so common of sinus disease.

DR. HOWARD LILIENTHAL, New York, N. Y.—May I say a word, too?

I think it was in 1918 that I operated upon a man for a left lower lobe bronchiectasis. I took the lobe out. I believed that the primary cause appeared to be a badly infected sinus. He had complete situs inversus, thoracic, at least.

That man was an intelligent individual. He was so afraid that I might operate upon the wrong side, judging by the x-ray alone, that he made me put a mark on his chest where I intended to operate. He was wise; he took no chances.

I am sorry to say that while he was temporarily cured, bronchiectatic suppuration appeared in his other lung. I sent him to Dr. Berck for x-ray treatment of his opposite side, not with the idea of curing his bronchiectasis but with the idea of stopping the discharge.

One other point. I don't like the use of the words "reversal of symmetry." If it is symmetrical, you can't reverse it. I would call it reversal of normal assymetry, which is what we are dealing with in the human being.

By the way, when operating upon the man referred to, I found he had the unusual marking of the middle lobe of the left lung, showing that it was indeed situs inversus of the thorax at least.

DR. HARRY C. BALLON, Montreal, Canada.—I should like to ask Dr. Churchill if any of these patients had any other congenital abnormalities other than the situs inversus of the heart. When I read the abstract of Dr. Churchill's paper, I looked for the occurrence of this triad in twins, but was unable to find any published examples.

I should like to ask if it is not fair to assume that individuals with situs inversus have a greater tendency to infection? Would it not be logical to assume, too, that an individual with situs inversus can develop bronchiectasis and nasal sinusitis just as well as any other individual, and that perhaps because of the situs inversus he is more susceptible, a more likely subject for bronchiectasis and nasal sinusitis? I take it that the bronchiectasis is of the acquired type.

DR. HANS C. JACOBAEUS, Stockholm, Sweden.—Personally, I have not seen such a case, but when I was at a meeting in Zürich, a professor described just such a case as you have, and he made a good explanation of congenital development of bronchiectasis.

DR. JOHN B. FLICK, Philadelphia, Pa.—I have had one patient with right lower lobe bronchiectasis and situs inversus on whom I did a lobectomy. This is the only case I have seen of that particular combination of conditions.

DR. LILIENTHAL.—Did he have sinus?

DR. FLICK.—He had chronic sinusitis.

DR. EDWARD D. CHURCHILL, Boston, Mass.—To answer Dr. Graham's question, these were cases of cylindrical bronchiectasis and not of cystic disease that is usually called congenital.

I accept Dr. Lilienthal's correction and shall review our embryologic nomenclature. It may be a little rusty.

Dr. Ballon raises the question that occurs to us all as to whether this is an anatomic maldevelopment, or whether it may be an immunologic maldevelopment. We do not know.

CYSTIC DISEASE OF THE LUNG*

Cure of a Solitary Cyst by Chemical Cauterization

William H. Field, M.D., F.A.C.S., and Lester Rosenberg, M.D.
Brooklyn, N. Y.

THOUGH until 1925 cases of congenital cystic disease of the lung had not been described in this country, Koontz's[1] excellent review of a large series of cases in that year and his compilation of a comprehensive bibliography appear to have stimulated interest in this condition. Since that time, several papers (Wood,[2] Hennell[3] and others) have appeared on this subject in which both the solitary and multiple type of lung cysts have been described. In none of the instances reported have we been able to find a case that exactly parallels our own, and for this reason and because the type of therapy successfully employed in our case had never been attempted before, we believe our experience is worth recording.

CASE REPORT

R. S., aged six and one-half months, was admitted to the Brooklyn Hospital, February 10, 1934, with the complaint of cough and dyspnea. At birth, July 26, 1933, an abnormality in the contour of the chest was noted, and when the infant was a few days old he began to breathe rapidly and laboredly. On August 4, 1933, he was taken to a hospital in the community where the family was then residing, where a diagnosis of empyema of the right chest was made on the basis of absent breath sounds, displacement of the heart to the left, and roentgenologic findings of opacity over the entire right lung from apex to base. At that hospital, an exploratory tap in the eighth interspace posterior to the midaxillary line was made and five ounces of milky white fluid, resembling chyle obtained. The fluid contained many lymphocytes, and the culture was sterile. The white blood count was 7,100, with polys 70 per cent, lymphocytes 23 per cent, and monocytes, 7 per cent. The hemoglobin was 105 per cent and the red blood count 4,020,000.

As the chest rapidly filled again, closed thoracotomy was performed on August 10, 1933, at which time a large amount of fluid was withdrawn. The fluid contained 1,860 cells, 80 per cent polys, and 20 per cent lymphs, and appeared "noninflammatory" in character. Only one colony of staphylococcus was obtained on culture and was thought to be a contamination. On August 17, 1933, x-ray showed no evidence of fluid, but pneumothorax was present on the right side. On September 1, 1933, partial collapse of the right lung was noted. The comment of the operating surgeons was that the cyanosis had been relieved and that the infant was definitely improved. There was profuse drainage from the wound which gradually lessened. The child was discharged from the hospital on September 5, 1933, with a note that the condition was probably due to obstruction of a large lymph vessel, with rupture into the right pleural cavity. After discharge, the infant gained fairly well, increasing from a weight of 7½ pounds on leaving the hospital to 12 pounds 9 ounces at six months. The cough, however, had returned, and the breathing again became labored and rapid.

*From the Departments of Surgery and Pediatrics, The Brooklyn Hospital, Brooklyn, N. Y.

At this time, on February 10, 1934, he was admitted to the Brooklyn Hospital. Physical examination revealed a fairly well-nourished infant with a marked keel-shaped protuberance of the lower end of the sternum. Though the breathing was rapid and labored, the epigastrium being retracted with each inspiration, the child did not appear acutely ill. The right chest was dull to percussion anteriorly and posteriorly. The left chest was hyperresonant. The breath sounds were totally absent anteriorly on the right side and much diminished posteriorly. There was a suggestion of a friction rub at the right base. The site of the old thoracotomy wound on the right side showed a healed scar. The heart was displaced to the left. The rhythm was regular and the sounds of good quality. There were no murmurs. The abdomen was normal. The temperature varied from normal to 101° F. X-ray on February 13, 1934, showed the right chest to be dense except for a streak of aeration at the base. The heart and mediastinal shadows were displaced to the left. There was an anomalous bony bridge between the fourth and fifth ribs in the posterior axillary line.

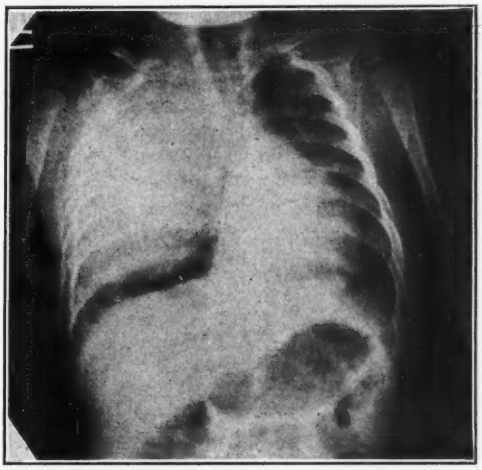

Fig. 1.—Feb. 17, 1934.

Our impression was that the condition was a congenital malformation of the thorax with fluid in the right chest. A neoplasm rather than infection was considered because, despite the marked pathology clinically and by x-ray, the child seemed relatively comfortable. An injury or malformation with rupture of the thoracic duct did not seem likely in view of the absence of emaciation and dehydration which usually accompany the loss of chyle. On February 16th, attempts to aspirate in the posterior axillary line between the fourth and fifth ribs and at another area just above the old thoracotomy scar were unsuccessful. On the following day, x-ray examination (Figs. 1, 2) showed the shadow in the right chest to lie posteriorly. We thought the condition now to be some congenital type of lung cyst, possibly dermoid.

On February 26, 1934, after first giving a blood transfusion, operation was performed under local anesthesia for cyst of the right lung. An incision was made from the posterior axillary line to the costal cartilage over the fifth rib. This was carried down through the muscles and through the periosteum. The rib was separated from the periosteum and excised. An incision was then made through the posterior periosteum, where instead of the pleura a layer of rather dense fatty-looking tissue

was encountered, about an eighth of an inch thick. There was apparently a very indefinite and adherent line of cleavage between the cyst wall above and the visceral pleura below which looked like the diaphragm, but was much too high to be the diaphragm. It was decided to cut through the cyst wall in order to explore its contents. A soft spongy lining material was encountered and within this a greenish mucoid, slightly foul, collection of about three ounces of pus. This was aspirated and the cavity flushed out with 1:1000 acriflavine solution, none of which appeared in the baby's mouth, though the head was well down throughout the operation. After exploring the cavity with the finger, however, the baby coughed up two or three drams of blood-tinged mucus. The cyst was found to occupy the upper half of the chest. Its lining wall felt smooth and soft as far as the finger could feel except for one small area in the axilla and above the incision which felt nodular. A specimen taken

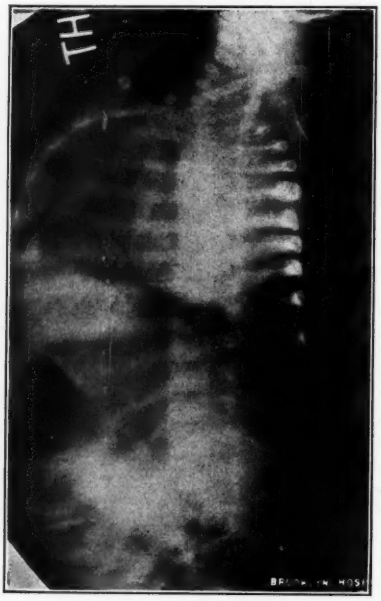

Fig. 2.—Feb. 17, 1934.

from this site with rongeur revealed what appeared to be cartilage. The heart could be felt pulsating, but each time the finger even gently touched this region, the child's pulse became weak and rapid and the respirations shallow.

It was decided that packing the cavity was impractical because touching the mediastinum caused too much disturbance. A vaseline gauze plug was, therefore, placed in the opening only and held by a silk suture and safety pin. This device allowed the discharge to escape and kept the wound edges apart. A vaseline flap valve was hung over the wound and a large fluffy dressing applied. The infant's condition at the end of the operation seemed better than before. His color was good and he seemed comfortable.

The pathologic specimen consisted of three small yellowish white fragments, which on histologic section showed vascular granulation tissue, containing large clear cells which appeared to be a foetal type of fat cell. No dermoid elements were present. The absence of a lining membrane was perhaps best explained on the presence of

secondary infection. In many instances only a single layer of cells lines a lung cyst, and it seems as if superimposed infection would readily account for its destruction.

A moderate amount of serosanguineous discharge was present on the dressing the day after operation and in the next few days lessened gradually. The child was somewhat improved and x-ray taken on March 2, 1934, showed the fluid in the right chest to be diminished. The area of density was markedly reduced in size, but the heart remained displaced to the left. Despite the child's good general condition and relative comfort, the heaving of the chest on inspiration and the labored character of the breathing persisted. It was decided to do a second-stage operation in an attempt to extirpate or destroy the cyst.

On March 5, 1934, the second operation was performed. The vaseline plug was removed from the wound, and following this the lung could be seen bulging up from

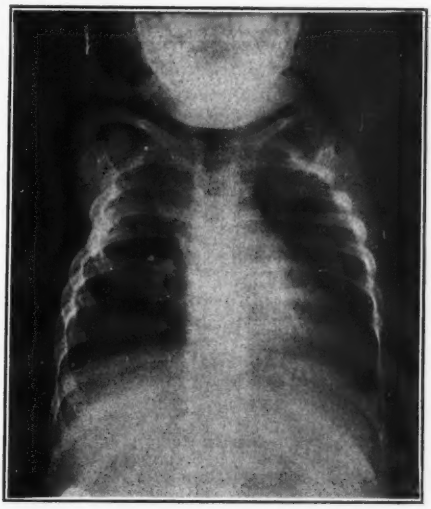

Fig. 3.—March 23, 1935.

below, almost entirely filling the cavity except for a fingerlike projection from the inner angle of the wound, caudad and medial, about the thickness of one's index finger and one and a half inches long. The whole cavity was lined with thickened substance, which shelled out in pieces with great ease. This was at first thought to be the lining of the cyst itself, but as the same kind of tissue was later found over most of the wound from the pleura out to the skin, it was thought to be merely coagulated lymph. The cyst lining was then scraped with a moderately sharp curette and the cavity lavaged with sterile water. No bronchial communication was present. The cavity was sponged out thoroughly with gauze and when dry was filled with 25 per cent silver nitrate solution. This was allowed to remain for about one and a half minutes and was then aspirated. The cavity was lavaged for two minutes with plain sterile water and finally with double strength saline. A vaseline pack to keep the wound edges open and a vaseline gauze flap-valve were applied.

The tissue removed at the second operation consisted of several fragments of brown coagulated material. Histologically, the sections showed a small area of vascular granulation tissue, the remainder being coagulated albuminous material.

On March 9, 1934, the pack was removed from the chest wall wound and the cavity lavaged with warm saline. What appeared to be flakes of silver nitrate mixed with coagulated material was obtained in the washings. The cavity held less than a half ounce. On March 12 the wound seemed closed and a Kelly clamp was inserted, allowing the escape of about one dram of clear serum. Percussion of the right chest gave a resonant note. On March 19, 1934, the wound was healed and the child was discharged, apparently cured. The breathing was normal, the dyspnea and heaving of the chest having disappeared.

One year later, on March 23, 1935, x-ray (Fig. 3) showed an area of density still present in the right chest extending up from the hilum, but the right lung was fully expanded. The scars of the operations were excellent. The lower sternum was still protuberant, but the right thorax appeared of equal capacity and function to the left chest. The percussion note was normal.

On January 3, 1936, examination revealed he had the development of a normal boy of his age. He had been symptom-free since discharge from the hospital, except for occasional head colds. The right chest was resonant, and the breath and voice sounds were normal. There had been no dyspnea or cyanosis at any time since his discharge from the hospital. The lower part of the sternum still protruded keel-shaped. Otherwise, he was normal in all respects except for hypertrophied tonsils and adenoids, removal of which was advised.

On November 3, 1936, his condition was good. He had been well since his previous visit. The right chest was resonant, and breath and voice sounds were normal. His activity had been that of other normal children of his age. There had been no cyanosis, dyspnea, or other difficulty.

CONCLUSION

Cure of a case of congenital solitary cyst of the lung in an infant, aged six and one-half months, treated by thoracotomy and application of 25 per cent silver nitrate solution, is reported.

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CINEFLUOROGRAPHY OF TODAY*

WILLIAM H. STEWART, M.D.
NEW YORK, N. Y.

BY cinefluorography is meant the making of a motion picture of the image seen on the fluoroscopic screen. Attempts were made to utilize this method soon after the discovery of the roentgen ray, but it has only been within the last five years that any marked measure of success has been forthcoming.

Recent developments in apparatus and x-ray equipment have greatly lessened the difficulties previously encountered and made possible films sufficiently sharp in detail to be of practical use.

It is the purpose of this paper to outline the technique of the method in use at Lenox Hill Hospital and to attempt to analyze its value on a basis of what has already been accomplished.

The following is a list of the equipment which we have been using:

1. A four-valve transformer, capable of giving a current of 125 K.V. plus 150 Ma. for a period of not less than five seconds.

2. An x-ray tube capable of taking 125 Ma. at 100 P.K.V. for not less than five seconds. The G.E. 10 R.W. is the best that can be obtained at the present time.

3. An upright fluoroscopic stand strong enough to support a heavy tube and with clearance sufficient to permit the use of high voltages.

The Screen-Film Combination.—It is impossible to consider the film and screen separately because both must be associated on the basis of two variables; likewise, the photographic film reacts not only to the intensity of the light but to the color as well. Similarly individual types of screens emit light of different color as well as of different intensity. In our experiments we have found the most satisfactory combination to be that of Eastman Panchromatic Super X film used in conjunction with a special yellow green zinc sulfide fluoroscopic screen developed by Levy and West, of London. The screen is similar to a Patterson type B.

The Lens.—A Zeiss Biotar F 0.85 lens was used and probably represents one of the most rapid which can be employed. It has a focal length of 5.5 cm.

The Camera.—A Bell and Howell 16 mm. model 70 D-filmo camera was employed. This camera had a special speed regulating attachment which made possible exposures at 4, 8, 12, 16, and 24 frames per second.

Technique.—The procedure in making the motion films is very simple. The patient is centered behind the fluoroscopic screen in the usual manner. The camera is mounted facing the screen and an exposure is made. The room is darkened and the camera started before the tube is

*From the Lenox Hill Hospital, New York.
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energized so that films are being taken the entire time that the patient is exposed to the x-ray.

In order to cover sufficient of the fluoroscopic screen to show an entire chest, it was necessary to use a camera screen distance of seven feet. For smaller areas, such as are suitable for the examination of a gallbladder or duodenum, three feet nine inches, or even less, may be used as the camera screen distance. The lens is used wide open.

The Exposure.—After the patient has been centered and the camera focused to cover the part of the screen which shows the parts to be examined, an exposure is made. For the thorax in a patient of average size, a five-second exposure is made at 125 Ma. and 100 K.V.P. The speed regulating device of the camera is set for 16 frames a second. This gives sufficient exposed film to permit the making of a loop with 80 frames, and at the same time shows the complete cycle of the circulatory organs of the chest.

For a moderately thin patient this will give films of normal exposure which, when projected, will show the motion of the thoracic structures exactly as they may be observed on the fluoroscopic screen.

With the equipment and technique described above we have been able to obtain excellent films of the action of the heart, lungs, diaphragm, and esophagus. A single five-second, 80-frame exposure is sufficient to record one complete respiratory cycle and two or three complete cardiac cycles. Films of the act of swallowing show the manipulation of the opaque bolus in the pharynx and its peristaltic descent through the esophagus.

Below the diaphragm we meet with some difficulties, especially in patients of advanced years and over 140 pounds in weight. In most cases, however, we are able to make a loop by shortening the distance to three feet nine inches and the number of frames per second to 4.

The entire action is contained on a strip of film containing from 20 to 80 frames, the projection of which would provide visible action for only a few seconds. By repeatedly printing this short film on a roll of film 100 feet in length, the cycles of action may be projected over and over again for many minutes. This provides ample time for study of the physiologic action of the organs under investigation.

The motion of the peristaltic wave through the length of the stomach takes at least forty seconds; consequently, it is not possible with our present technique to show a complete cycle. However, if three runs are made of five seconds each, the film obtained can be joined in a loop in such a way that the illusion of continuous motion and cyclic activity of the stomach is produced. Since the exposure is made at one-fourth the normal rate, the motion seen when the film is projected is four times as fast as is seen on the fluoroscopic screen. This, however, is not a distinct disadvantage because it is often easier for the eye to detect abnormalities in the peristalsis at this increased rate than it is at the normal rate on the screen.

ADVANTAGES OF CINEFLUOROGRAPHY

By means of cinefluorography a permanent record may be made of the appearance and motion of functioning organs and parts of the body, such as the heart, lungs, diaphragm, esophagus, stomach, and joints. By serial repeated printing on a continuous film, the action may be projected for as long a time as desired. This motion picture record of the behavior of the organs can be studied at leisure indefinitely without danger of excessive exposure of the patient or the examiner. The permanent motion picture record provides a means of comparing the patient's condition or function with previous motion picture records, thus demonstrating the effects of treatment or the natural evolution of the disease process. It provides, therefore, a means for building up a library of excellent teaching material. These motion picture films can be shipped to distant places for consultation and opinion on the condition of the patient at the present time or at any time in his previous history as represented on the films.

The procedure is simple, convenient, and safe. With further experimentation and improvement the scope of the method doubtless will be broadened.

FIELD FOR FUTURE IMPROVEMENT

At its present stage of development, the greatest needs in the field of cinefluorography are:

1. A method of prolonging the exposure so that a record of twenty to thirty seconds of action may be made at one time.
2. A more brilliant fluoroscopic screen.
3. X-ray tubes of greater capacity for longer periods.
4. More sensitive film.
5. Better correspondence between the sensitivity of the film and the light production of the screen.

The first of these needs, namely, prolonging the exposure, can be met by installing a rotating contact breaker, switching the high tension on and off in synchronism with the camera shutter. This allows a tube rest during the period when the film is moving and the shutter of the camera is closed. Since the time of the motion of the film and the duration of the stationary period are of approximately equal length, the exposure time can be doubled without further tube strain. This is the method advocated by Reynolds of London. Up to the present time we make a five-second run, give the tube a fifteen-second rest, repeat the five-second exposure, give a further tube rest of fifteen or twenty seconds, and then make a final run of five seconds more, making a total film exposure of fifteen seconds. This technique works satisfactorily except in reproducing the gastric motility at its normal rate.

Improvements in screen, x-ray tubes, and films must await developments by the chemists and physicists. Until they are available we must

learn to make the best possible use of the remarkable materials and equipment which they have already placed in our hands.

SUMMARY

Cinefluorography is the making of a motion picture record of the image seen on the fluoroscopic screen.

The patient is placed behind the fluoroscopic screen as in the ordinary fluoroscopic examination. The screen image is photographed by a motion picture camera equipped with a special lens.

The method is particularly effective in recording the action of the heart, lungs, esophagus, diaphragm, and joints. Because of physical limitations, it is less successful in slow-moving organs, such as those located below the diaphragm.

Cinefluorography furnishes a permanent record of the function and motion of a part and permits a leisurely study of this record without danger to the patient or the examiner. This record can be compared with previous films to show the progress of the condition. It may be sent to a distant consultant for opinion. A collection of such film records provides valuable teaching material. It is probably destined to become an important division of roentgenologic investigation and diagnosis.

DISCUSSION

DR. HOWARD LILIENTHAL, New York, N. Y.—I should like to ask Dr. Stewart what the chances are in the reasonably near future of making a slow picture so that you can watch deliberately the motion of the organs.

DR. DUANE CARR, Memphis, Tenn.—I should like to ask Dr. Stewart a question regarding a few of the details: What film is he using, and what protection has he for the camera so the film is not fogged by the x-rays?

DR. WILLIAM H. STEWART, New York, N.Y.—The question as to the most satisfactory 16 mm. film to use in this work has already been answered in the paper. It is the Eastman Super X.

The reason the unexposed film in a camera during a run does not become fogged is apparently due to the protection afforded by a large lead glass which is placed in front of the screen. We are careful to keep the camera directly back of the center of this glass. The greatest difficulty so far has been to obtain an x-ray tube which will stand 100 K.V. and 125 Ma. for more than five seconds. The best we can do at the present time is the G. E. 10 R. W. The manufacturers of this tube allow us to use five seconds at the above setting, a tube rest of fifteen seconds, a second run of five seconds, further tube rest of fifteen seconds, and then a final run of five seconds more. The total exposure time is thus fifteen seconds. This is ample to cover a complete cycle on all organs except the stomach. The three runs are then spliced together. From this loop a print is made of as many feet as desired.

In answer to Dr. Lilienthal's question, I would say that the normal speed of movie film is 16 frames to the second. In order to obtain slow reproduction it is necessary to make at least 24 frames to the second, which is rather difficult unless the patient is unusually favorable. The projectors are all made for normal 16-frame reproductions. To slow them down without a flicker is also difficult.

Department of Reviews and Abstracts

CONDUCTED BY DUFF S. ALLEN, M.D., ASSOCIATE EDITOR

Selected Abstracts

Pulmonary Embolism, A Statistical Investigation of Its Incidence in Twelve London Hospitals in the Decade, 1925-34, Robin Pilcher. Brit. J. Surg. **25**: 42, 1937.

The impression that pulmonary embolism had a seasonal or epidemic incidence stimulated the author to analyze postmortem records of 731 cases of fatal pulmonary embolism.

No evidence was found to indicate a seasonal or epidemic incidence. However, the following information was obtained: of the 731 cases, 537 followed operation, 36 followed accidental injuries, and in 158 instances there was no accidental operative trauma. In the group of cases having pulmonary embolism following injury, none followed injuries involving the upper extremities. The interval between death in fatal cases of pulmonary embolism following trauma varied from one to more than twenty-eight days. The supposed primary thrombosis in traumatic cases was found in veins of the right leg more commonly than the left. There seemed to be an association between right-sided injuries and operations and thrombosis of veins of the right leg. The maximum age incidence was between the ages of fifty-five and fifty-nine years. There was an equal number of male and females in nontraumatic cases. In the traumatic cases females were in the majority. The findings suggested that more important than the nature of the illness or trauma was the immobilization of the patient.

Brian Blades.

The Development of the Terminal Air Passages of the Human Lung. W. G. Barnard and T. D. Day. J. Path. & Bact. (Pathological Society of Great Britain and Ireland) **45**: 67, 1937.

The lungs of 48 human fetuses were studied in an effort to trace the developmental changes which lead to striking alteration in the histologic picture as compared to the adult. In the early fetal lung the embryonic anlage of the air passages is completely lined with epithelium; in an adult such epithelium can only be undisputably seen in the bronchi and distal branches of the bronchial tree.

The lungs consist of undifferentiated mesenchyme, containing a few capillaries and a few scattered tubes representing bronchi in the early fetal months. During the third month of fetal life large tubular spaces are present in the lungs lined by pseudostratified epithelium separated by abundant mesenchyme. At the fourth month the epithelium is differentiated into two types. The larger spaces are lined by pseudostratified columnar epithelium; some of these are lined by cartilage and smooth muscle. Continuous with these are smaller branching tubules which end in almost spherical vesicles. The epithelium lining the terminal vesicles and the small branches is made up of approximately cubical cells with prominent outlines. It is quite distinct and differs in appearance from the epithelium lining the fetal bronchi. Epithelium of this type is not found in the adult. At the beginning of the fifth fetal month the capillaries are more numerous. There is an increase in the branching and ramification of the epithelial tubules and their terminal vesicles. During the fifth month the capillaries around the blood vessels are more numerous. Toward the end of the fifth month the capillaries start to push between epithelial cells and reach the lumina of the vesicles.

The tendency of the capillaries to penetrate the epithelium becomes more marked toward the end of the sixth month. The epithelium degenerates and desquamates into the lumina of the potential air spaces. The terminal air spaces gradually take on the adult appearance. A few epithelial cells may be present in sections of full time stillbirths, but in infants who have breathed for a short time no trace of epithelium is found.

It is concluded that the epithelial lining of the terminal air passages begins to disappear toward the end of the fifth fetal month and does not reappear. The lung does not change essentially in structure after the end of the sixth fetal month.

Findings and opinions of other investigators concerning development of the lung are discussed.

There are excellent drawings and photomicrographs illustrating histologic changes described in the article.

Brian Blades.

Pulmonary Pneumatocele (Localized Alveolar or Lobular Ectasia) Certain Considerations in Cystic Disease of the Lung. Carleton B. Peirce and Paul R. Dirske. Radiol. **28**: 651, 1937.

The term "congenital cystic disease" now applied to a wide variety of pulmonary changes is not accepted by the authors. They suggest that the roentgen diagnosis be classified under four main titles.

1. True congenital cysts.
2. (a) Chronic interstitial pneumonitis with emphysema.
   (b) Chronic bullous emphysema.

3. Cystic bronchiectasis.

4. Pulmonary pneumatocele (localized alveolar or lobular ectasia).

True congenital cysts are rare in reported cases, and while the biologic possibility is admitted, attention is called to the fact that demonstration of congenital cystic changes in the postnatal lung is rare.

Chronic interstitial pneumonitis with emphysema may follow bronchopneumonia or unresolved lobar pneumonia where interstitial inflammatory changes have caused alveolar emphysema that may become cystic in proportions. Such a process tends to be lobar or unilateral and rarely contains fluid.

Chronic bullous emphysema developing in an asthmatic due to expiratory obstruction by bronchospasm may present a roentgenographic picture of multiple cysts.

The frequency of lobular pneumonia in infants and pulmonary changes resulting from inflammatory changes is considered a more logical explanation of cystic bronchiectasis than assuming the presence of a congenital abnormality.

Pulmonary pneumatocele (localized alveolar or lobular ectasia) is represented by a single or a few contiguous grossly emphysematous alveoli. These ectasic air spaces may assume massive proportions. Acute lobular emphysema associated with lobular pneumonia is believed by the authors to be the origin of the pneumatocele.

Attention is called to the fact that in the majority of reported cases the inflammatory changes have been greatest in the lung tissue intervening between dilated air spaces, as compared to the cystic areas themselves. The authors feel that if the "cysts" were the source of infection this would not be the case.

Case reports and roentgenograms are included, illustrating the types described in the article.

Brian Blades.

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